```
=> d his

     (FILE 'REGISTRY' ENTERED AT 09:44:03 ON 18 AUG 2003)
               DEL HIS Y

     FILE 'REGISTRY' ENTERED AT 09:46:29 ON 18 AUG 2003
               ACT ANTDERIV/A
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L1   (      4751)SEA FILE=REGISTRY ABB=ON  PLU=ON  3406.1/RID
L2   (    480663)SEA FILE=REGISTRY ABB=ON  PLU=ON  46.157.1/RID
L3           581 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND L1
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     FILE 'HCAPLUS' ENTERED AT 09:47:31 ON 18 AUG 2003
L4          1356 S L3
L5          2951 S ANT OR ADENOSINE NUCLEO? TRANSLOC?
L6             3 S L4 AND L5
L7           235 S ATRACTYLOSID?
L8             3 S L7 AND L5
L9             5 S L5 (L) LIGAND?
L10            8 S L6 OR L8 OR L9
L11         1387 S L4 OR L7
L12           29 S L11 (L) (LABEL? OR RADIO? OR FLUORES? OR EU##)
L13       479001 S SOLID
L14            3 S L11 (L) L13
L15            1 S L11 (L) IMMOBIL?
L16           12 S L14 OR L15 OR L10
L17           12 S L5 AND LIGAND#
L18            7 S L17  NOT L16
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FILE 'REGISTRY' ENTERED AT 09:52:30 ON 18 AUG 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   15 AUG 2003  HIGHEST RN 567484-39-3
DICTIONARY FILE UPDATES:  15 AUG 2003  HIGHEST RN 567484-39-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d que l3
L1   (      4751)SEA FILE=REGISTRY ABB=ON  PLU=ON  3406.1/RID
L2   (    480663)SEA FILE=REGISTRY ABB=ON  PLU=ON  46.157.1/RID
L3           581 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 AND L1


=> d scan
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:l3
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:end

=> d scan l3

L3    581 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS on STN
IN    19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[(4'-hydroxy[1,1'-
      biphenyl]-4-yl)carbonyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-
      glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI)
MF    C43 H54 O18 S2

Absolute stereochemistry.
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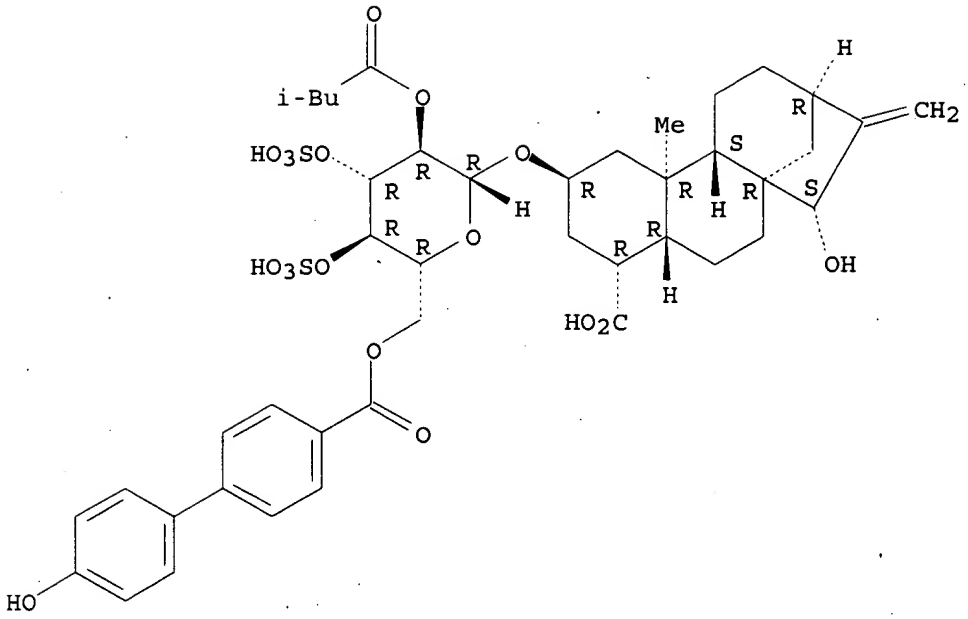
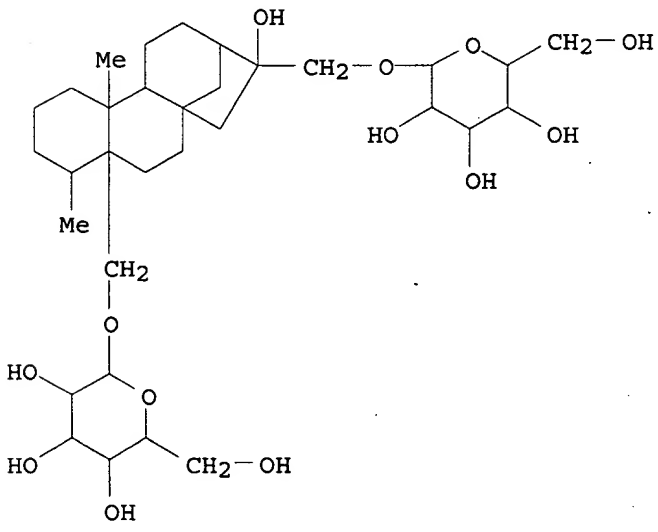


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 581 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN .beta.-D-Glucopyranoside, (4.alpha.,16.alpha.)-16-hydroxykaurane-17,18-diyl bis- (9CI)
MF C32 H54 O13



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

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FILE 'HCAPLUS' ENTERED AT 09:53:01 ON 18 AUG 2003
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FILE COVERS 1907 - 18 Aug 2003  VOL 139 ISS 8
FILE LAST UPDATED: 17 Aug 2003  (20030817/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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     (FILE 'REGISTRY' ENTERED AT 09:46:29 ON 18 AUG 2003)
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     FILE 'HCAPLUS' ENTERED AT 09:47:31 ON 18 AUG 2003
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L5          2951 S ANT OR ADENOSINE NUCLEO? TRANSLOC?
L6             3 S L4 AND L5
L7           235 S ATRACTYLOSID?
L8             3 S L7 AND L5
L9             5 S L5 (L) LIGAND?
L10            8 S L6 OR L8 OR L9
L11         1387 S L4 OR L7
L12           29 S L11 (L) (LABEL? OR RADIO? OR FLUORES? OR EU##)
L13       479001 S SOLID
L14            3 S L11 (L) L13
L15            1 S L11 (L) IMMOBIL?
L16           12 S L14 OR L15 OR L10
L17           12 S L5 AND LIGAND#
L18            7 S L17  NOT L16

     FILE 'REGISTRY' ENTERED AT 09:52:30 ON 18 AUG 2003

     FILE 'HCAPLUS' ENTERED AT 09:53:01 ON 18 AUG 2003

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L16  ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2002:185165  HCAPLUS
DOCUMENT NUMBER:          136:243571
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TITLE: Mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active molecules having the ability to alter and/or prevent and/or mimic the interaction of Vpr with **ANT**

INVENTOR(S): Jacotot, Etienne Daniel Francois; Kroemer, Guido; Roques, Bernard Pierre; Edelmann, Lena; Hoebeke, Johan; Brenner-Jan, Catherine; Belzacq, Anne-Sophie

PATENT ASSIGNEE(S): Institut Pasteur, Fr.; Centre National de la Recherche Scientifique; Institut National de la Sante et de la Recherche Medicale - INSERM; Universite de Technologie de Compiegne

SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020570	A2	20020314	WO 2001-EP11316	20010911
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002015004	A5	20020322	AU 2002-15004	20010911
US 2002068273	A1	20020606	US 2001-949650	20010912

PRIORITY APPLN. INFO.: US 2000-231539P P 20000911
US 2000-232841P P 20000915
WO 2001-EP11316 W 20010911

AB The invention is directed to the induction of mitochondrial membrane permeabilization via the phys. and functional interaction of the HIV-1 proapoptotic Vpr protein with the mitochondrial inner membrane protein ANT (adenine nucleotide translocator, also called adenine nucleotide translocase or ADP/ATP carrier). HIV-1 Vpr (viral protein R) interacts with the permeability transition pore complex (PTPC) to trigger ANT pore formation and/or mitochondrial membrane permeabilization and consequent cell death. Reagents and methods fo inducing and/or inhibiting the binding of Vpr to ANT, mitochondrial membrane permeabilization, and apoptosis are provided.

IC ICM C07K014-155
CC 6-1 (General Biochemistry)
Section cross-reference(s): 1, 10, 14
ST HIV1 Vpr protein **ANT** mitochondria membrane permeabilization apoptosis
IT Transport proteins
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(ADP/ATP carrier; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**
)
IT Proteins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bcl-2; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Biological transport
(antiport; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Lipids, biological studies
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(bilayer membrane or liposome; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Membrane, biological
(bilayer, planar; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Proteins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene vpr; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Diagnosis
(genetic; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Anti-AIDS agents
Apoptosis
Cell death
Drug screening
Fluorescent indicators
Human
Human immunodeficiency virus 1
Liposomes
Molecular association
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Ion channel
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Peptides, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Mitochondria
(membrane; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols.

altering, preventing or mimicking interaction of Vpr with **ANT**
)

IT Membrane, biological
(mitochondrial; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**
)

IT Diagnosis
(mol.; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT Biological transport
(permeation, channel-mediated; mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT 403842-76-2
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

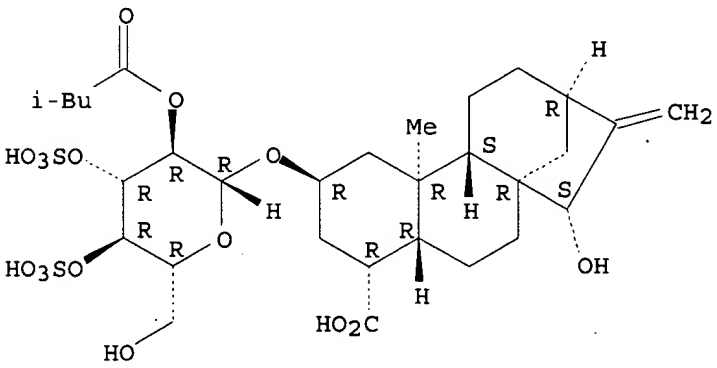
IT 10465-78-8, Diamide **17754-44-8**, **Atractyloside**
72093-21-1, Mastoparan
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

IT **17754-44-8**, **Atractyloside**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism of mitochondrial membrane permeabilization by HIV-1 Vpr, mimetics of Vpr and methods of screening active mols. altering, preventing or mimicking interaction of Vpr with **ANT**)

RN 17754-44-8 HCAPLUS

CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, dipotassium salt, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



2 K

L16 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:833514 HCAPLUS
DOCUMENT NUMBER: 136:1609
TITLE: Production of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor
INVENTOR(S): Anderson, Christen M.; Davis, Robert E.; Clevenger, William; Wiley, Sandra Eileen; Miller, Scott W.; Szabo, Tomas R.; Ghosh, Soumitra S.; Moos, Walter H.; Pei, Yazhong; Carroll, Amy K.
PATENT ASSIGNEE(S): Mitokor, USA
SOURCE: PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085944	A2	20011115	WO 2001-US15416	20010511
WO 2001085944	A3	20020829		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1283884	A2	20030219	EP 2001-935420	20010511

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 2000-569327	A	20000511
	WO 2001-US15416	W	20010511

OTHER SOURCE(S): MARPAT 136:1609

AB Compns. and methods are provided for producing adenine nucleotide translocator (ANT) polypeptides and fusion proteins, including the prodn. and use of recombinant expression constructs having a regulated promoter. ANT ligands and compns. and methods for identifying ANT ligands, agents that bind ANT and agents that interact with ANT are also disclosed. Thus, ANT cDNAs were expressed in Sf9 and E.coli. Fluorescent and radiolabeled derivs. of atractyloside were prepd. Binding of these derivs. to ANT was examd.

IC ICM C12N015-12
ICS C12N015-62; C07K014-705; C07K016-28; G01N033-53; G01N033-58; G01N033-60; G01N033-68; C07H015-203
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1
ST **atractyloside** fluorescent radiolabeled deriv synthesis; adenine nucleotide translocator human prodn insect mammalian cell
IT Transport proteins
RL: ANT (Analyte); ARG (Analytical reagent use); BPN (Biosynthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ADP/ATP carrier; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands**

and screening assays therefor)

IT Escherichia coli
(**ANT** DNA expression in; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT Cattle
Mouse
Rat
(**ANT** of human or; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT Animal cell line
(SF9, **ANT** prodn. with recombinant; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(anti-**ANT**; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT Trichoplusia ni
(cell, **ANT** prodn. with recombinant; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT **Ligands**
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(for **ANT**, labeled with fluorophores, radioisotopes, or biotin; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT Molecular cloning
(of **ANT** DNA; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT Mitochondria
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT 374777-22-7
RL: PRP (Properties)
(Unclaimed; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT 108778-97-8P 113285-74-8P 125724-85-8P
RL: ANT (Analyte); ARG (Analytical reagent use); BPN (Biosynthetic preparation); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT **267886-33-9P 267886-35-1P 267886-37-3P**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT 51-67-2, Tyramine 98-59-9, Toluenesulfonyl chloride 108-30-5, Succinic

anhydride, reactions 501-97-3, 3-(4-Hydroxyphenyl)propionic acid 578-58-5, 2-Methylanisole 3443-45-6, 1-Pyrenebutyric acid 16712-64-4, 6-Hydroxy-2-naphthoic acid **17754-44-8, Atractyloside** 34071-95-9 50995-74-9 **267886-34-0 267886-55-5 374064-29-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT 33446-14-9P, 3-(4-Methoxy-3-methylbenzoyl)propionic acid 33446-15-0P, 4-(4-Methoxy-3-methylphenyl)butyric acid **267886-39-5P 267886-48-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT 13811-11-5P 19374-20-0P 53937-19-2P **84882-67-7P 267886-16-8P 267886-17-9P 267886-18-0P 267886-19-1P 267886-21-5P 267886-32-8P 267886-36-2P 267886-38-4P 267886-40-8P 267886-41-9P 267886-42-0P 267886-43-1P 267886-44-2P 267886-45-3P 267886-46-4P 267886-47-5P 267886-49-7P** 267886-54-4P **268557-13-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

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374661-74-2 374661-75-3 374661-76-4 374661-77-5 374661-78-6
374661-79-7 374661-80-0 374661-81-1 374661-82-2 374661-83-3
RL: PRP (Properties)
(unclaimed nucleotide sequence; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

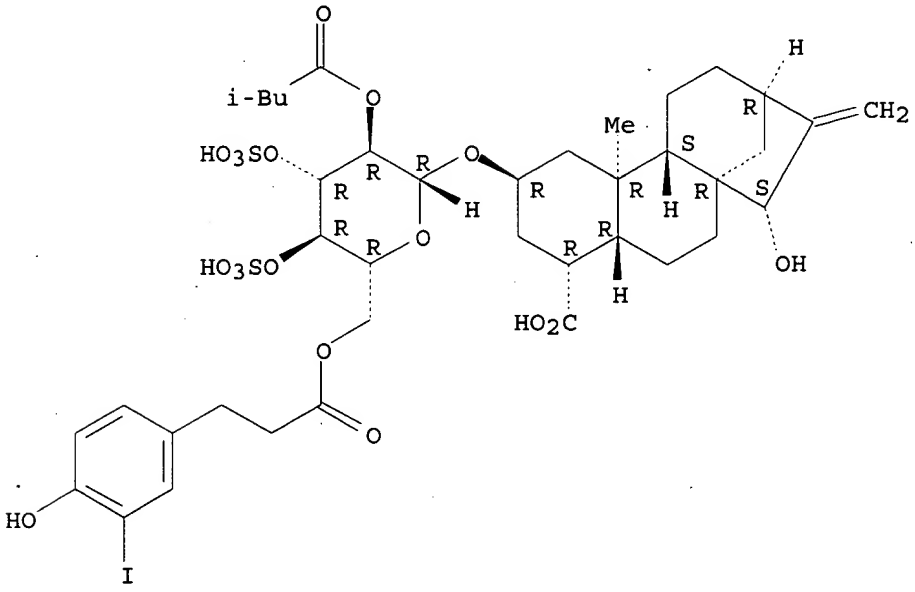
IT 268230-34-8 374777-20-5 374777-21-6
RL: PRP (Properties)
(unclaimed sequence; prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

IT **267886-33-9P 267886-35-1P 267886-37-3P**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

RN 267886-33-9 HCAPLUS

CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[3-(4-hydroxy-3-iodophenyl)-1-oxopropyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

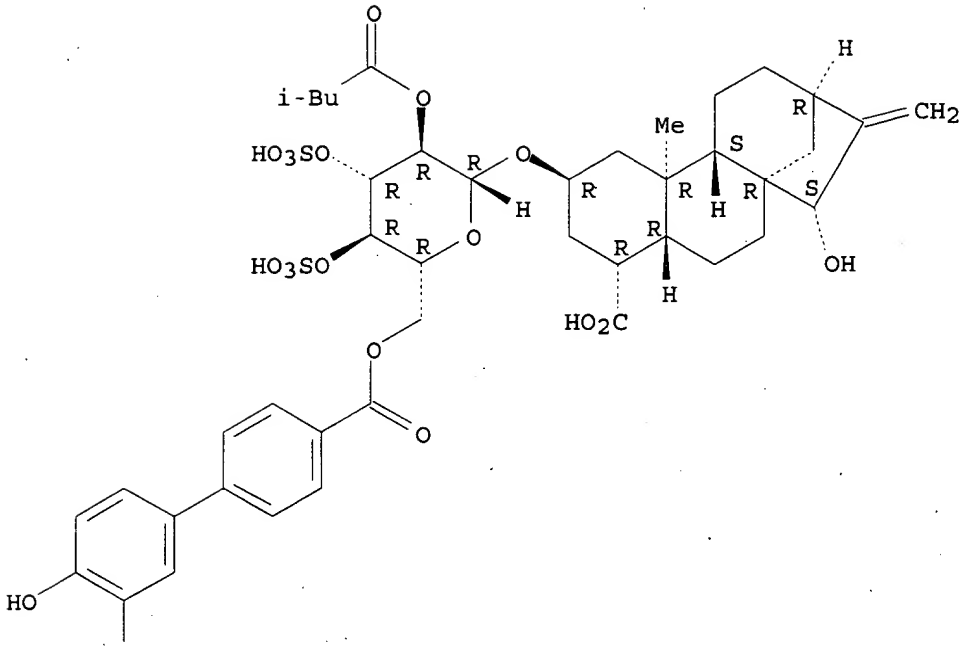


RN 267886-35-1 HCAPLUS

CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[(4'-hydroxy-3'-iodo[1,1'-biphenyl]-4-yl)carbonyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

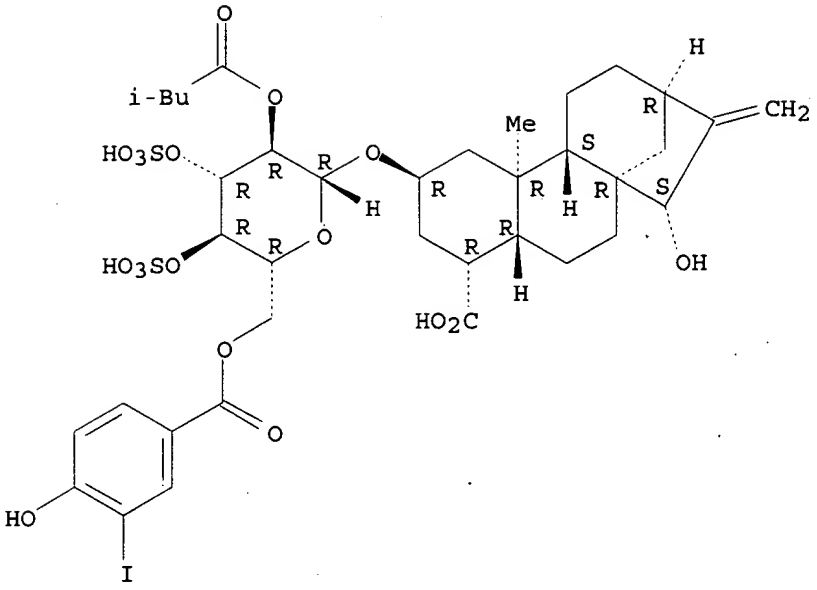
PAGE 1-A



PAGE 2-A

RN 267886-37-3 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-(4-hydroxy-3-iodobenzoyl)-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

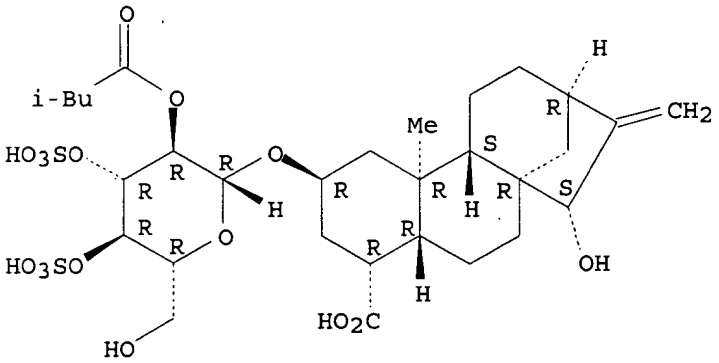


IT **17754-44-8, Atractyloside 267886-34-0**
267886-55-5 374064-29-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

RN 17754-44-8 HCAPLUS

CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, dipotassium salt, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

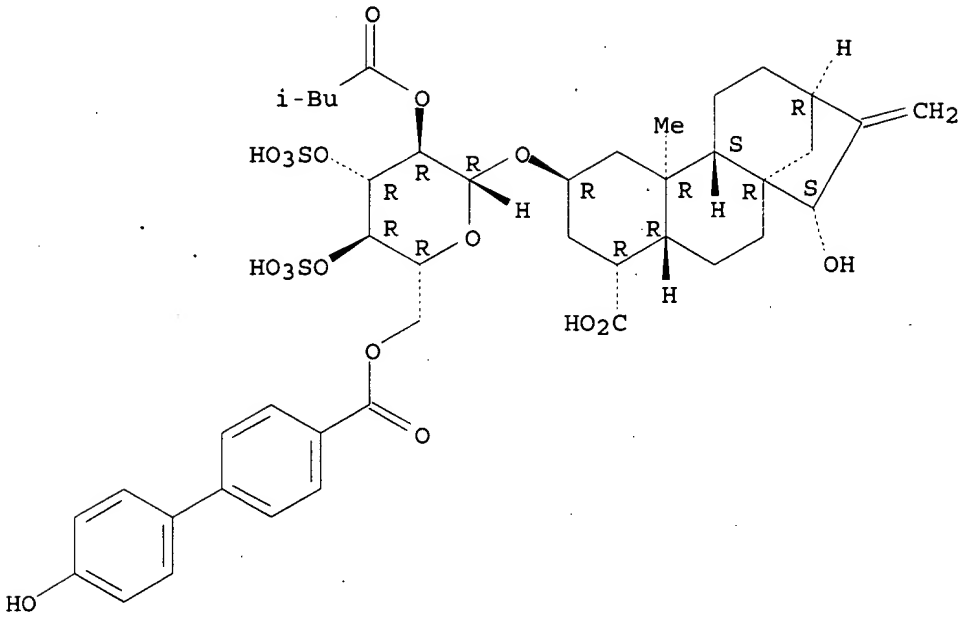


●2 K

RN 267886-34-0 HCAPLUS

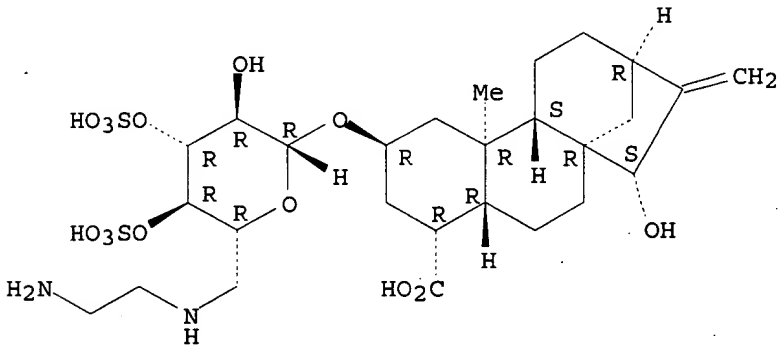
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[(4'-hydroxy[1,1'-biphenyl]-4-yl)carbonyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 267886-55-5 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 2-[[6-[(2-aminoethyl)amino]-6-deoxy-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-15-hydroxy-, (2.beta.,4.alpha.,15.alpha.)- (9CI). (CA INDEX NAME)

Absolute stereochemistry.



RN 374064-29-6 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, dipotassium salt, trihydrate, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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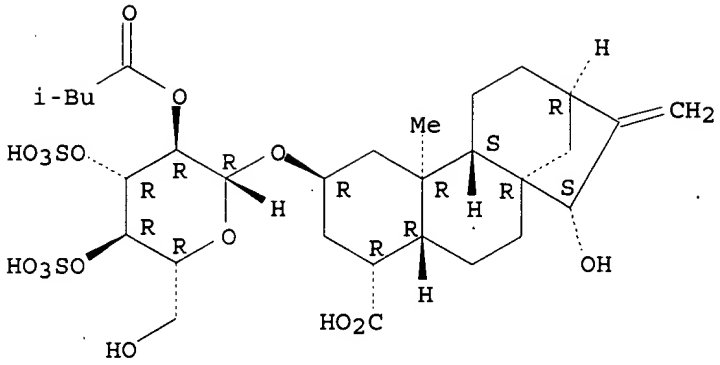

●2 K

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●3 H_2O

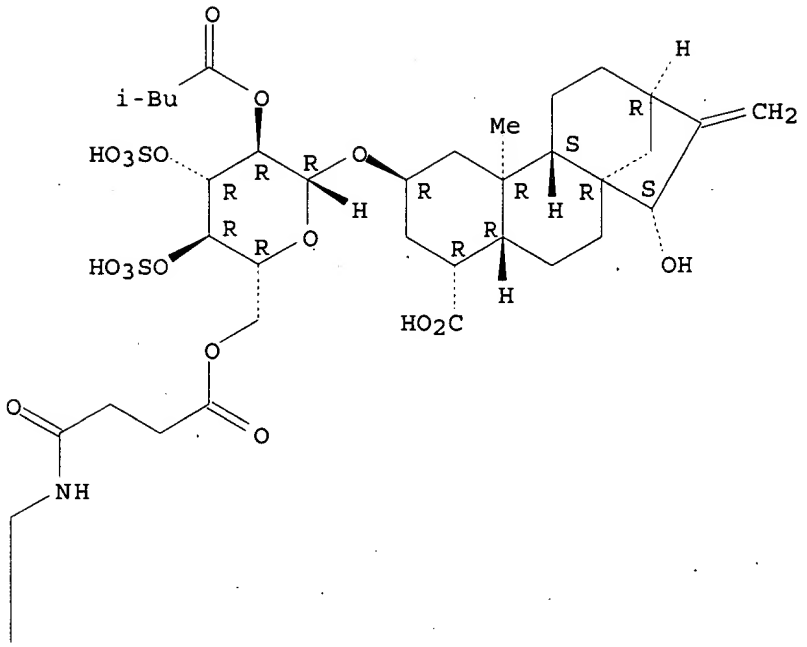
IT **267886-39-5P 267886-48-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

RN 267886-39-5 HCAPLUS

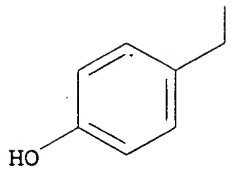
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[4-[[2-(4-hydroxyphenyl)ethyl]amino]-1,4-dioxobutyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

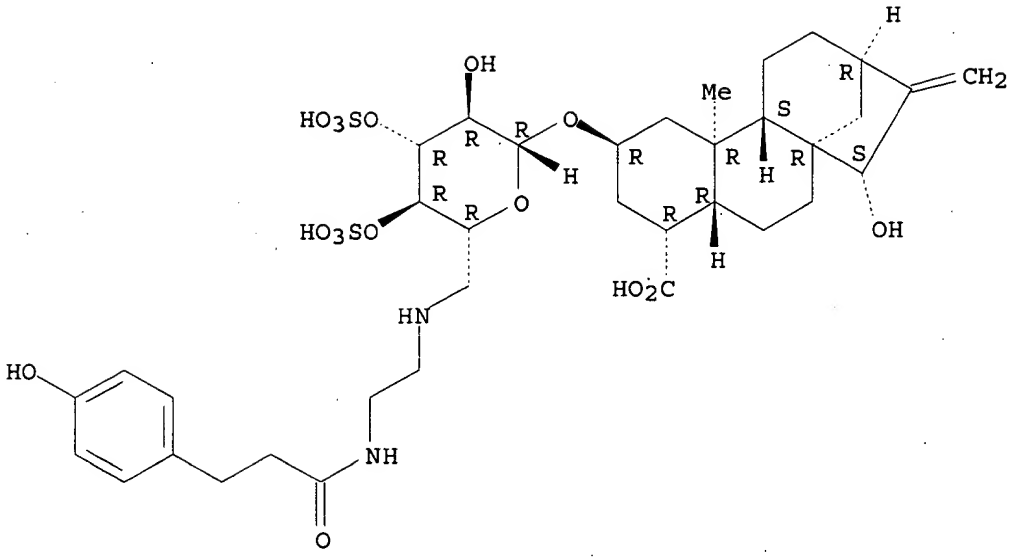


PAGE 2-A



RN 267886-48-6 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 2-[[6-deoxy-6-[[2-[[3-(4-hydroxyphenyl)-1-oxopropyl]amino]ethyl]amino]-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-15-hydroxy-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

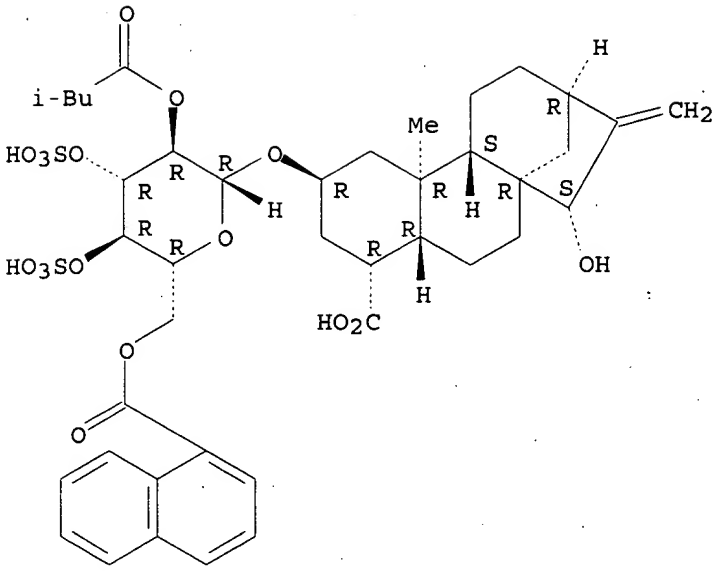


IT **84882-67-7P 267886-16-8P 267886-17-9P**
267886-18-0P 267886-19-1P 267886-21-5P
267886-32-8P 267886-36-2P 267886-38-4P
267886-40-8P 267886-41-9P 267886-42-0P
267886-43-1P 267886-44-2P 267886-45-3P
267886-46-4P 267886-47-5P 267886-49-7P
268557-13-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prodn. of adenine nucleotide translocator (**ANT**) with recombinant cells, **ANT ligands** and screening assays therefor)

RN 84882-67-7 HCAPLUS

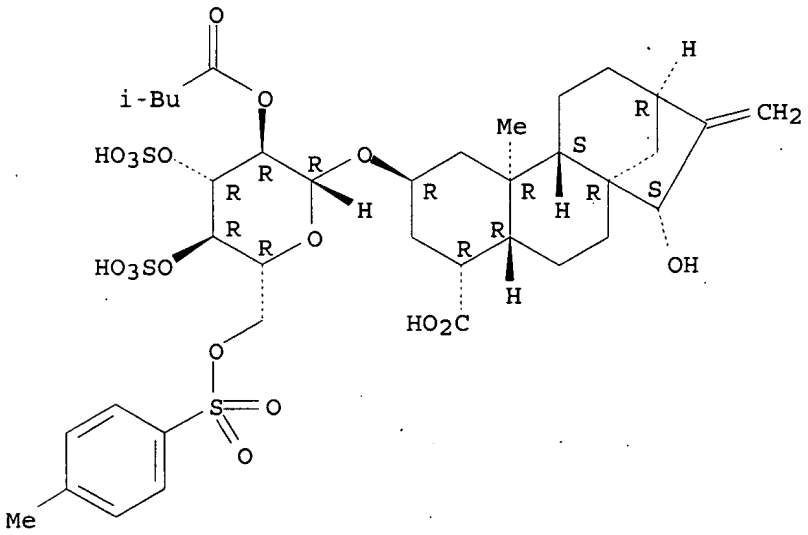
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-6-O-(1-naphthalenylcarbonyl)-2,3-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



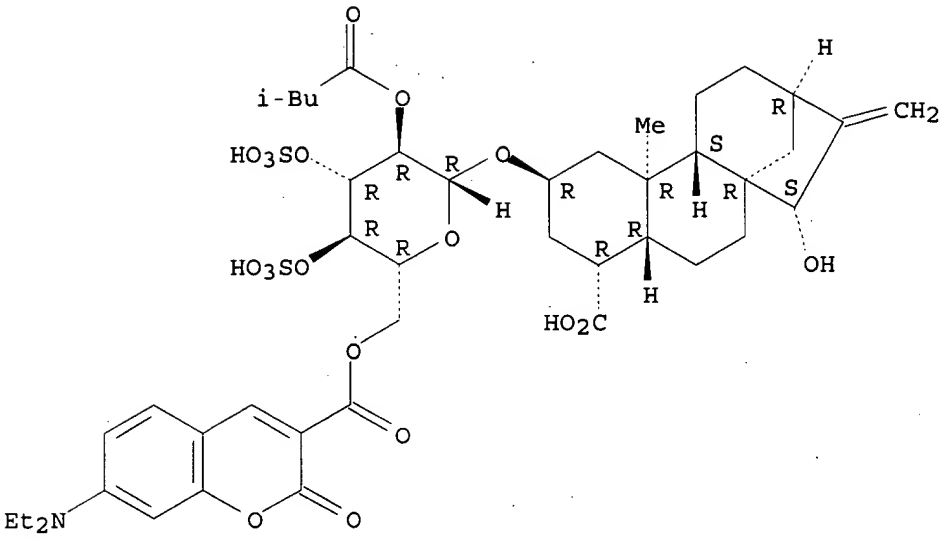
RN 267886-16-8 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-6-O-[(4-methylphenyl)sulfonyl]-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



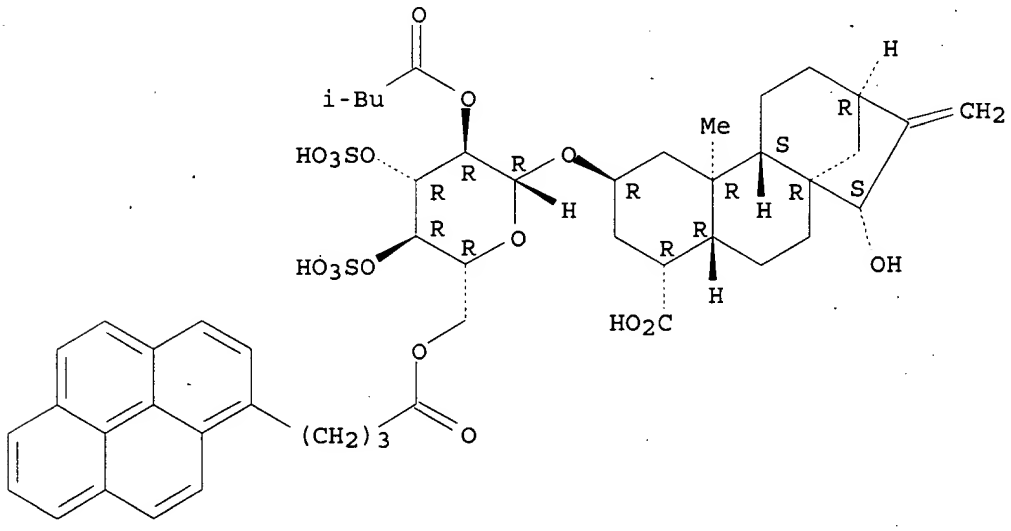
RN 267886-17-9 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 2-[[6-O-[[7-(diethylamino)-2-oxo-2H-1-benzopyran-3-yl]carbonyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-15-hydroxy-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



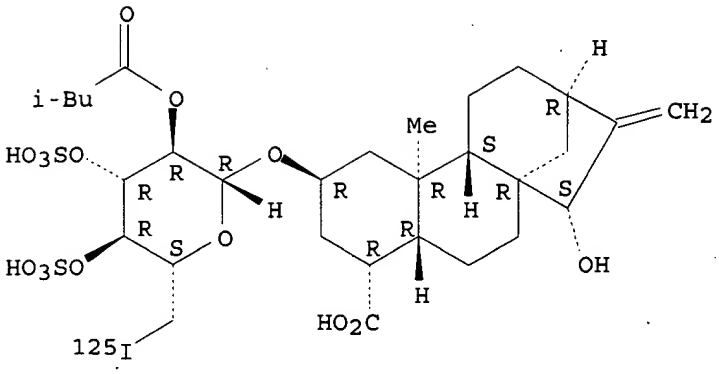
RN 267886-18-0 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-6-O-[1-oxo-4-(1-pyrenyl)butyl]-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



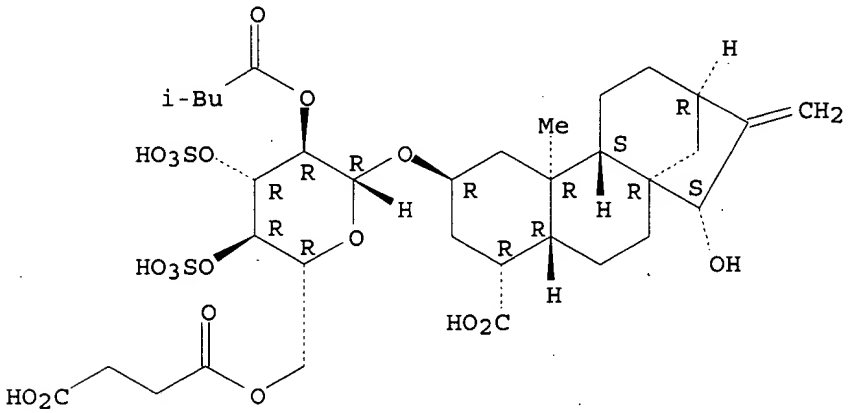
RN 267886-19-1 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 2-[[6-deoxy-6-(iodo-125I)-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-15-hydroxy-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 267886-21-5 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 2-[[6-O-(3-carboxy-1-oxopropyl)-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-15-hydroxy-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

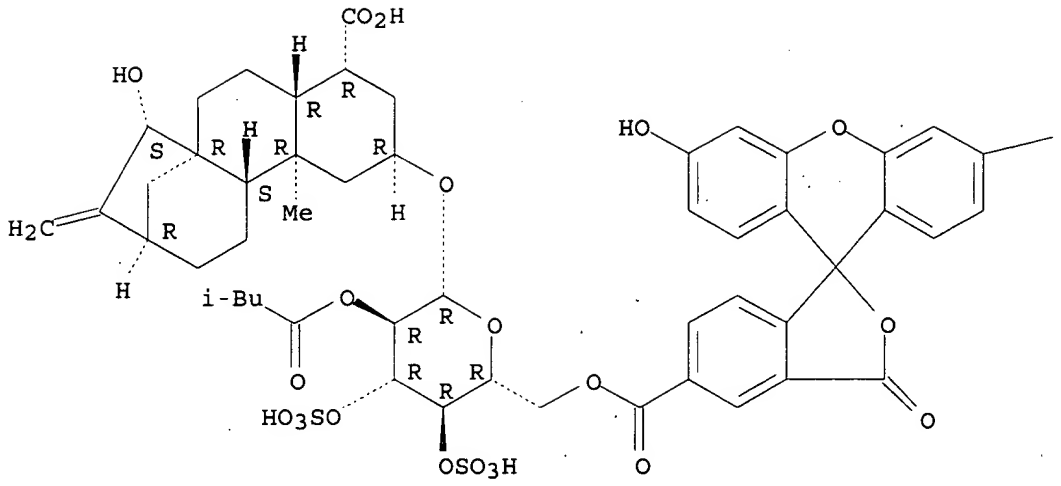
Absolute stereochemistry.



RN 267886-32-8 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 2-[[6-O-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)carbonyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-15-hydroxy-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

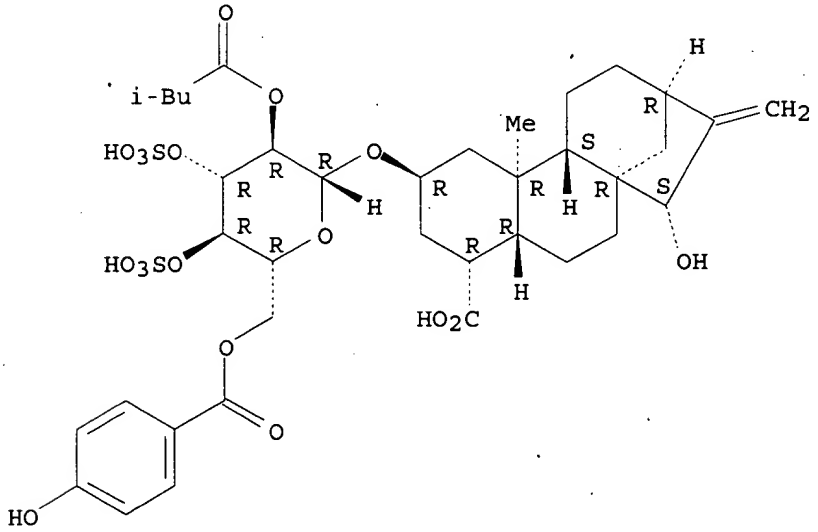


PAGE 1-B

—OH

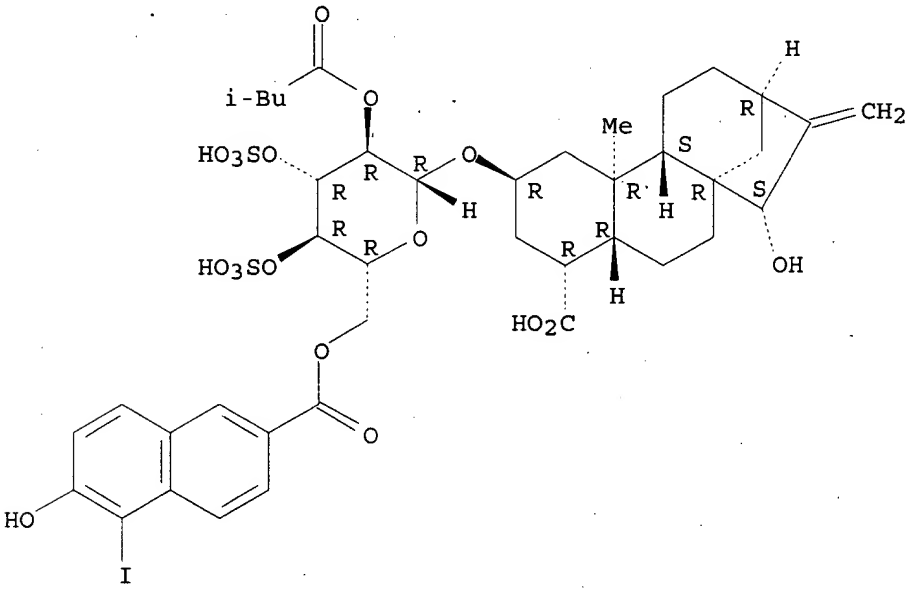
RN 267886-36-2 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-(4-hydroxybenzoyl)-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 267886-38-4 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[(6-hydroxy-5-iodo-2-naphthalenyl)carbonyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

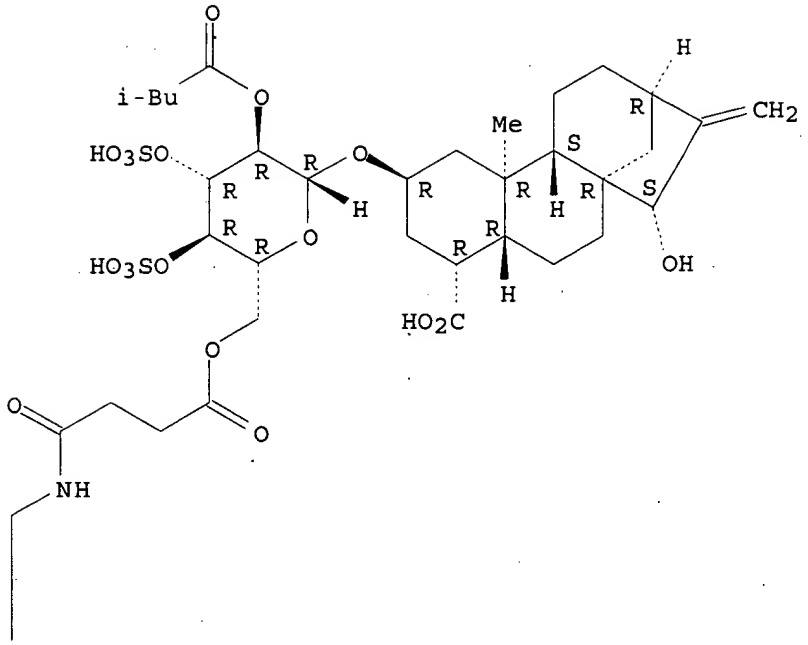
Absolute stereochemistry.



RN 267886-40-8 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[4-[[2-(4-hydroxy-3-iodophenyl)ethyl]amino]-1,4-dioxobutyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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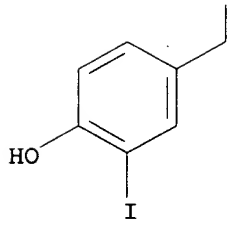
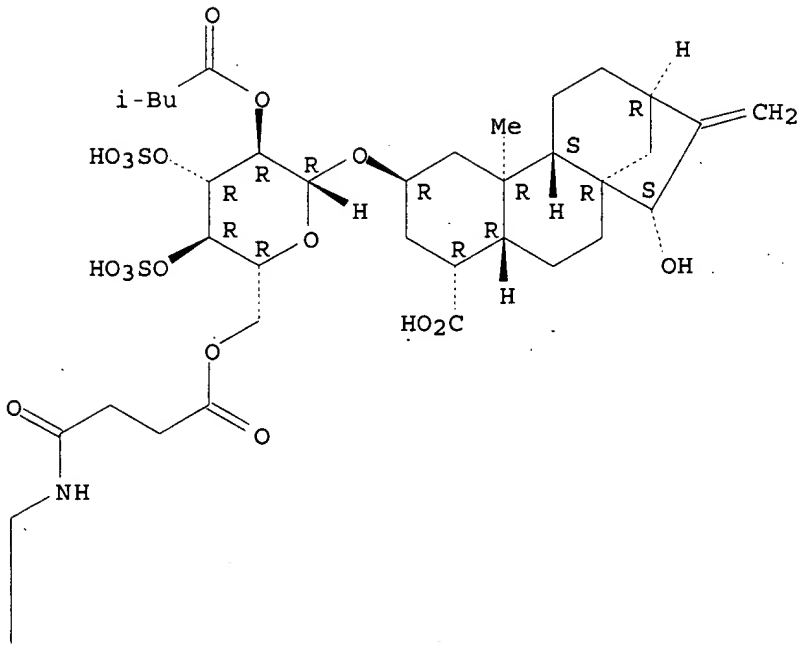


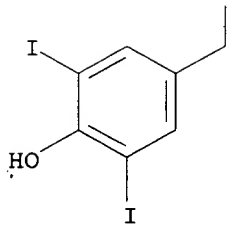
RN 267886-41-9 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[4-[[2-(4-hydroxy-3,5-diiodophenyl)ethyl]amino]-1,4-dioxobutyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

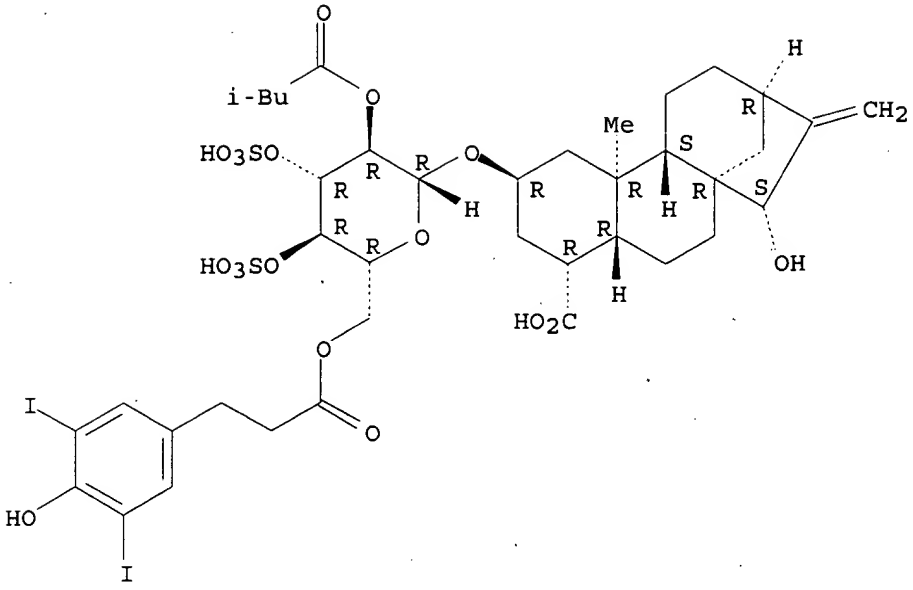


PAGE 2-A



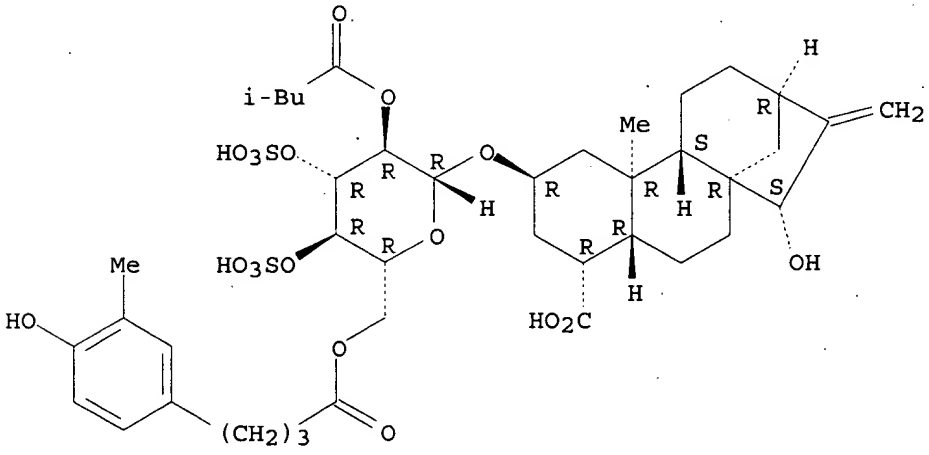
RN 267886-42-0 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[3-(4-hydroxy-3,5-diiodophenyl)-1-oxopropyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



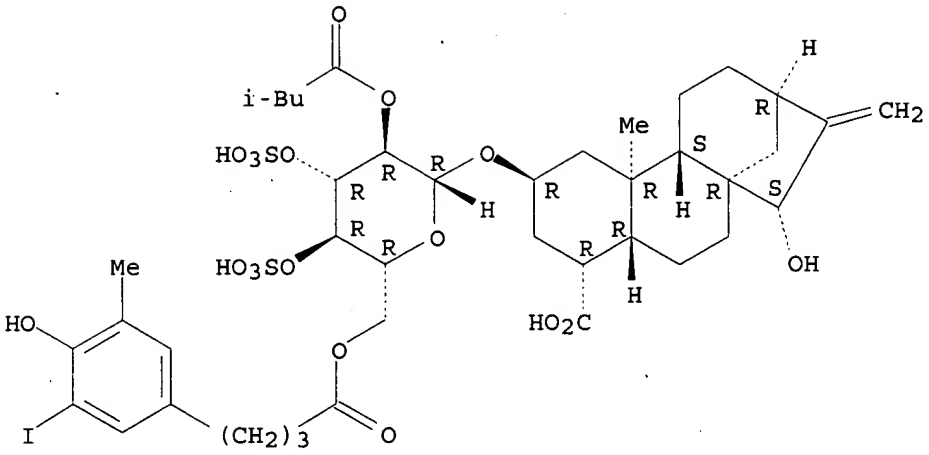
RN 267886-43-1 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[4-(4-hydroxy-3-methylphenyl)-1-oxobutyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



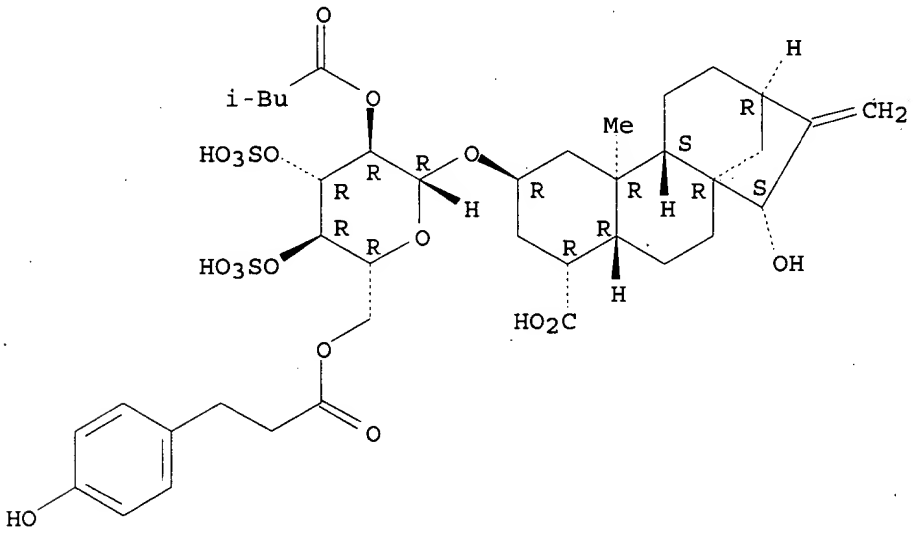
RN 267886-44-2 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[4-(4-hydroxy-3-iodo-5-methylphenyl)-1-oxobutyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



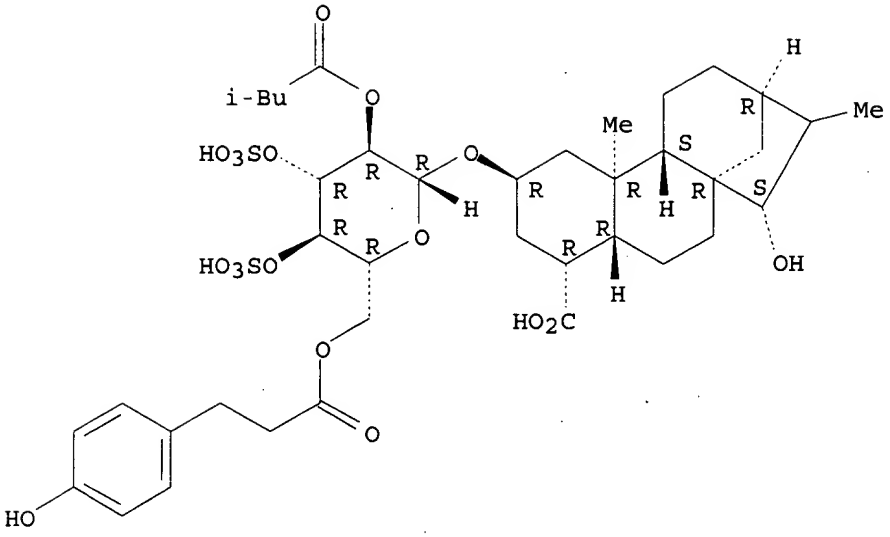
RN 267886-45-3 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 15-hydroxy-2-[[6-O-[3-(4-hydroxyphenyl)-1-oxopropyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



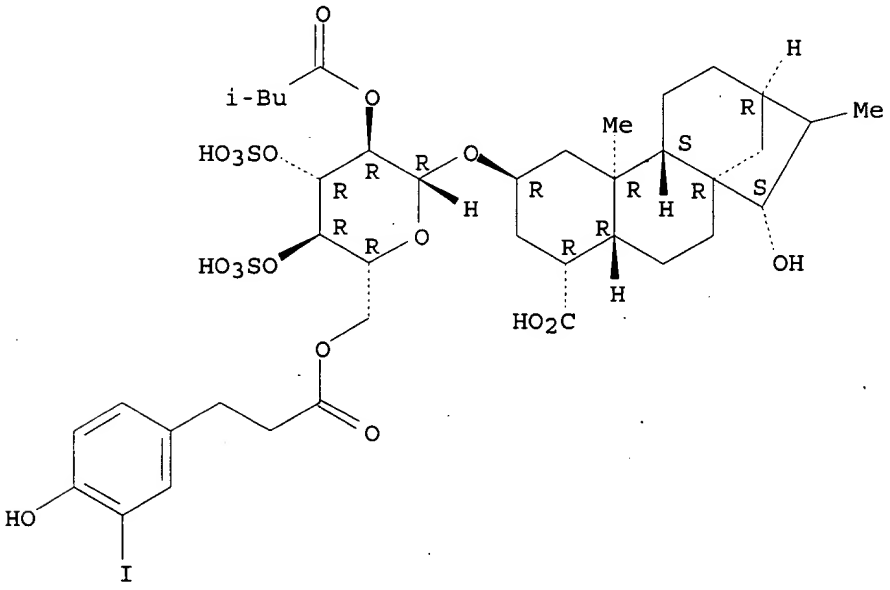
RN 267886-46-4 HCAPLUS
CN 19-Norkauran-18-oic acid, 15-hydroxy-2-[[6-O-[3-(4-hydroxyphenyl)-1-oxopropyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.,16.xi.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



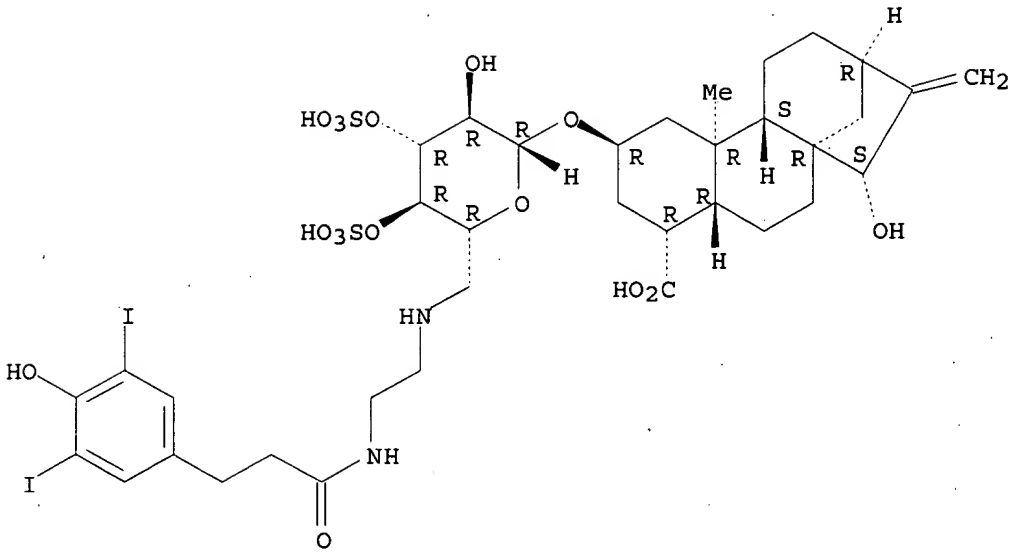
RN 267886-47-5 HCAPLUS
CN 19-Norkauran-18-oic acid, 15-hydroxy-2-[[6-O-[3-(4-hydroxy-3-iodophenyl)-1-oxopropyl]-2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.,16.xi.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



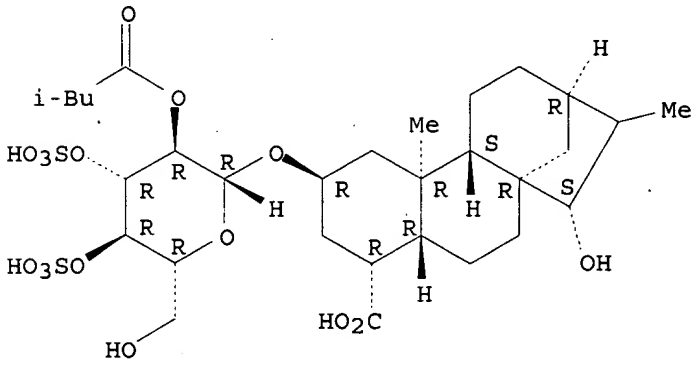
RN 267886-49-7 HCAPLUS
CN 19-Norkaur-16-en-18-oic acid, 2-[[6-deoxy-6-[[2-[[3-(4-hydroxy-3,5-diiodophenyl)-1-oxopropyl]amino]ethyl]amino]-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-15-hydroxy-, (2.beta.,4.alpha.,15.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 268557-13-7 HCAPLUS
CN 19-Norkauran-18-oic acid, 15-hydroxy-2-[[2-O-(3-methyl-1-oxobutyl)-3,4-di-O-sulfo-.beta.-D-glucopyranosyl]oxy]-, (2.beta.,4.alpha.,15.alpha.,16.xi.)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:676999 HCAPLUS
DOCUMENT NUMBER: 135:252790
TITLE: Single nucleotide polymorphisms in human genes
INVENTOR(S): Cargill, Michele; Ireland, James S.; Lander, Eric S.
PATENT ASSIGNEE(S): Whitehead Institute for Biomedical Research, USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001066800	A2	20010913	WO 2001-US7268	20010307
WO 2001066800	A3	20030605		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002032319	A1	20020314	US 2001-801274	20010307

PRIORITY APPLN. INFO.: US 2000-187510P P 20000307
US 2000-206129P P 20000522

AB The invention provides nucleic acid segments of the human genome, particularly nucleic acid segments from genes including polymorphic sites. The polymorphisms were identified by resequencing of target sequences from individuals of diverse ethnic and geog. backgrounds by hybridization to probes immobilized to microfabricated arrays. Some of the single nucleotide polymorphisms (SNPs) specify a different amino acid sequence, some are silent or are in noncoding regions, and some specify a stop signal in protein translation. Allele-specific primers and probes hybridizing to regions flanking or contg. these sites are also provided. The nucleic acids, primers and probes are used in applications such as phenotype correlations, forensics, paternity testing, medicine and genetic anal.

IC ICM C12Q001-68
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 13

L16 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:449813 HCAPLUS
DOCUMENT NUMBER: 135:18821
TITLE: Solid mixture of food contents and food additives, procedures for its production and use of the same.
INVENTOR(S): Janssen, Evelyn; Schmidt, Ralf
PATENT ASSIGNEE(S): Nutrinova Nutrition Specialties & Food Ingredients G.m.b.H., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19961338	A1	20010621	DE 1999-19961338	19991217
WO 2001043568	A1	20010621	WO 2000-EP12468	20001209

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1241953	A1	20020925	EP 2000-983270	20001209

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003516740	T2	20030520	JP 2001-544515	20001209
US 2002197372	A1	20021226	US 2002-148941	20020606

PRIORITY APPLN. INFO.: DE 1999-19961338 A 19991217
WO 2000-EP12468 W 20001209

AB The invention concerns a solid mixt. of food contents and additives, whereby the mixt. consists of .gtoreq.1 thermoplastic ductile matrix material and .gtoreq.1 food additive stored in this matrix material.

IC ICM A23L001-03
ICS A23L001-09; A23L001-236

CC 17-6 (Food and Feed Chemistry)

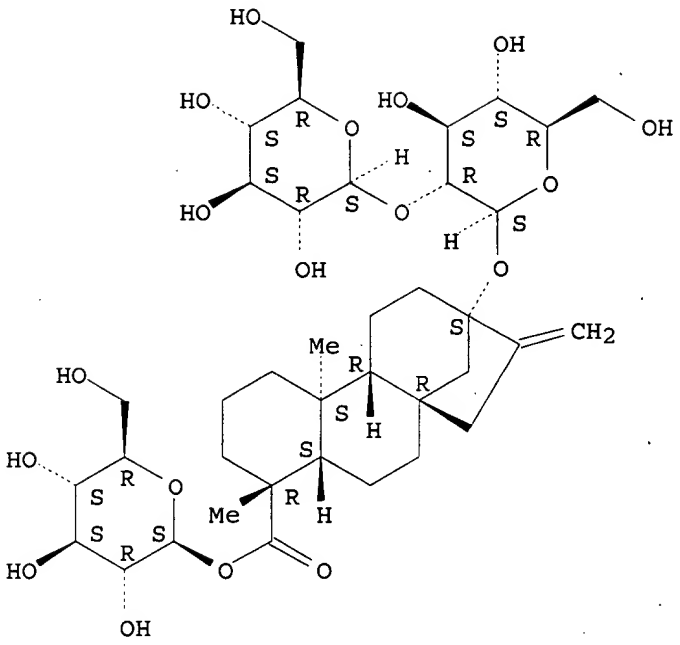
IT 50-70-4, Sorbitol, biological studies 50-99-7, D-Glucose, biological studies 57-48-7, D-Fructose, biological studies 57-48-7D, D-Fructose, oligo derivs., biological studies 57-50-1, Sucrose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 69-79-4, Maltose 77-92-9, Citric acid, biological studies 81-07-2, Saccharin 87-69-4, Tartaric acid, biological studies 87-81-0, D-Tagatose 87-99-0, Xylitol 100-88-9, Cyclamate 110-17-8, Fumaric acid, biological studies 128-44-9, Saccharin sodium 139-05-9, Sodium cyclamate 149-32-6, Erythritol 585-86-4, Lactitol 585-88-6, Maltitol 6915-15-7, Malic acid 7664-38-2, Phosphoric acid, biological studies 9005-80-5, Inulin 9050-36-6, Maltodextrin 20702-77-6, Neohesperidin dihydrochalcone 22839-47-0, Aspartame, 34612-38-9, Maltotetraose 55589-62-3, Sunett 56038-13-2, Sucralose **57817-89-7**, Stevioside 64519-82-0, Isomalt 80182-41-8, Glucosylsucrose 80863-62-3, Alitame 87419-56-5, Lactosucrose 165450-17-9, Neotame
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(**solid** mixt. of food contents and food additives, procedures for its prodn. and use of the same.)

IT **57817-89-7**, Stevioside
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(**solid** mixt. of food contents and food additives, procedures for its prodn. and use of the same.)

RN 57817-89-7 HCAPLUS

CN Kaur-16-en-18-oic acid, 13-[(2-O-.beta.-D-glucopyranosyl-.beta.-D-glucopyranosyl)oxy]-, .beta.-D-glucopyranosyl ester, (4.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:320839 HCAPLUS
DOCUMENT NUMBER: 135:74298
TITLE: Responses of the **ant** lasius niger to various compounds perceived as sweet in humans: A structure-activity relationship study
AUTHOR(S): Tinti, Jean-Marie; Nofre, Claude
CORPORATE SOURCE: Faculty of Medicine of Lyon Laennec, University of Lyon 1, Lyon, Fr.
SOURCE: Chemical Senses (2001), 26(3), 231-237
CODEN: CHSED8; ISSN: 0379-864X
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A behavioral study on the ant Lasius niger was performed by observing its feeding responses to 85 compds. presented in a two-choice situation (tested compd. vs. water control or sucrose soln.). Among these compds., only 21 were phagostimulating: six monosaccharides (D-glucose, 6-deoxy-D-glucose, L-galactose, L-fucose, D-fructose, L-sorbose), four derivs. of D-glucose (Me .alpha.-D-glucoside, D-gluconolactone and 6-chloro- and 6-fluoro-deoxy-D-glucose), five disaccharides (sucrose, maltose, palatinose, turanose and isomaltose), one polyol glycoside (maltitol), three trisaccharides (melezitose, raffinose and maltotriose) and two polyols (sorbitol and L-iditol). None of the 16 non-carbohydrate non-polyol compds. tested, although perceived as sweet in humans, was found to be active in ants. The molar order of effectiveness of the major naturally occurring compds. (melezitose > sucrose = raffinose > D-glucose > D-fructose = maltose = sorbitol) is basically different from the molar order of their sweetness potency in humans (sucrose > D-fructose > melezitose > maltose > D-glucose = raffinose = sorbitol). On a molar basis melezitose is in L. niger about twice as effective as sucrose or raffinose, while D-glucose and D-fructose are three and four times less effective, resp., than sucrose or raffinose. From a structure-activity

relationship study it was inferred that the active monosaccharides and polyols should interact with the ant receptor through only one type of receptor, through the same binding pocket and the same binding residues, via a six-point interaction. The high effectiveness of melezitose in L. niger mirrors the feeding habits of these ants, which attend homopterans and are heavy feeders on their honeydew, which is very rich in this carbohydrate.

CC 12-6 (Nonmammalian Biochemistry)

ST **ant** feeding sweetness carbohydrate structure activity

IT Feeding
Lasius niger
Structure-activity relationship
Sweetness
(a structure-activity relationship study of responses of **ants** to various compds. perceived as sweet in humans)

IT Carbohydrates, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(a structure-activity relationship study of responses of **ants** to various compds. perceived as sweet in humans)

IT 50-69-1, D-Ribose 50-70-4, D-Glucitol, biological studies 50-99-7, D-Glucose, biological studies 56-81-5, Glycerol, biological studies 57-48-7, D-Fructose, biological studies 57-50-1, Sucrose, biological studies 58-86-6, D-Xylose, biological studies 59-23-4, D-Galactose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 69-79-4, Maltose 81-07-2, Saccharin 87-79-6, L-Sorbose 87-81-0, D-Tagatose 87-89-8, myo-Inositol 87-99-0, Xylitol 97-30-3, Methyl .alpha.-D-glucoside 99-20-7, Trehalose 107-21-1, Ethylene glycol, biological studies 139-05-9, Sodium cyclamate 140-46-5, Suosan 146-72-5, 3-O-Methyl-D-glucose 149-32-6, Erythritol 154-17-6, 2-Deoxy-D-glucose 470-55-3, Stachyose 488-45-9, L-Iditol 488-81-3, Adonitol 488-82-4, D-Arabitol 492-61-5, .beta.-D-Glucose 492-62-6, .alpha.-D-Glucose 492-93-3, 1,5-Anhydro-D-mannitol 499-40-1, Isomaltose 512-69-6, Raffinose 528-50-7, Cellobiose 533-67-5, 2-Deoxy-D-ribose 547-25-1, Turanose 551-68-8, D-Psicose 551-84-8, D-Xylulose 585-86-4, Lactitol 585-88-6, Maltitol 585-99-9, Melibiose 597-12-6, Melezitose 608-66-2, Galactitol 609-06-3, L-Xylose 617-04-9, Methyl .alpha.-D-mannoside 642-38-6, Quebrachitol 709-50-2 921-60-8, L-Glucose 1109-28-0, Maltotriose 1114-34-7, D-Lyxose 1198-69-2, D-Gluconolactone 1990-29-0, D-Altrose 2106-10-7, .alpha.-D-Glucopyranosyl fluoride 2319-57-5, L-Threitol 2418-52-2, D-Threitol 2438-80-4, L-Fucose 2490-91-7, 3-Deoxy-D-glucose 2595-97-3, D-Allose 2595-98-4, D-Talose 3458-28-4, D-Mannose 3615-37-0, D-Fucose 3615-41-6, L-Rhamnose 4205-23-6, D-Gulose 4536-08-7 4618-18-2, Lactulose 5978-95-0, D-Idose 7643-75-6, L-Arabitol 7658-08-4, 6-Deoxy-D-glucose 10323-20-3, D-Arabinose 13718-94-0, Palatinose 15572-79-9, L-Galactose 20408-97-3, 5-Thio-D-glucose 20702-77-6, Neohesperidin dihydrochalcone 22839-47-0, Aspartame 30950-27-7, Perillartine 40656-44-8, 6-Chloro-6-deoxy-D-glucose 55589-62-3, Acesulfamepotassium 56038-13-2, Sucralose **57817-89-7**, Stevioside 74390-15-1, Cyanosuosan 80863-62-3, Alitame 116869-55-7 135507-50-5, Superaspartame 160955-43-1, Dulcin 165450-17-9, Neotame 186308-88-3, Magap
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(a structure-activity relationship study of responses of **ants** to various compds. perceived as sweet in humans)

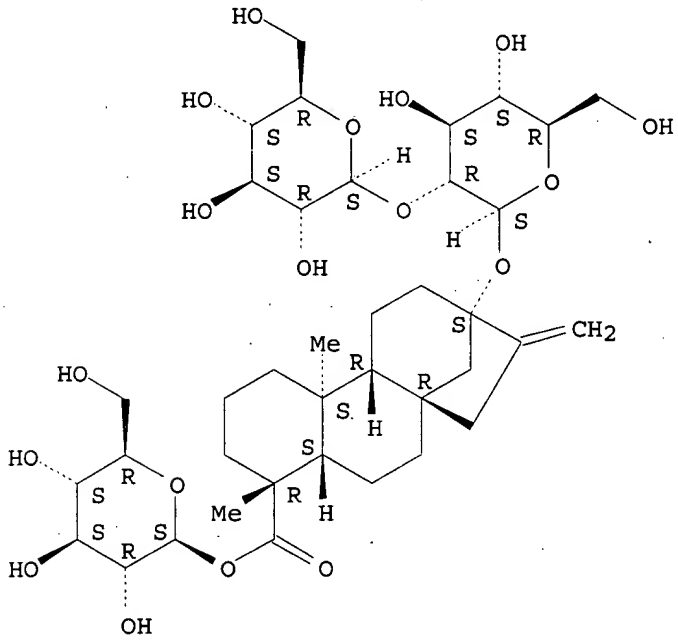
IT **57817-89-7**, Stevioside
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(a structure-activity relationship study of responses of **ants** to various compds. perceived as sweet in humans)

RN 57817-89-7 HCAPLUS

CN Kaur-16-en-18-oic acid, 13-[(2-O-.beta.-D-glucopyranosyl-.beta.-D-glucopyranosyl)oxy]-, .beta.-D-glucopyranosyl ester, (4.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:101291 HCAPLUS

DOCUMENT NUMBER: 134:161880

TITLE: cDNAs encoding the Flt-3 receptor ligand and there use as adjuvants in vector vaccines

INVENTOR(S): Hermanson, Gary George

PATENT ASSIGNEE(S): Vical Inc., USA

SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009303	A2	20010208	WO 2000-US20679	20000731
WO 2001009303	A3	20010816		

W: CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-146170P P 19990730

AB A method of increasing the strength of the immune response of vector

vaccines using an expression vector for the Flt3 ligand is described. The vaccines are made of independent non-integrating expression vectors: one encodes the antigen or a cytokine and the other encodes the Flt3 ligand. The present invention also provides a method broadly directed to improving immune response of a vertebrate in need of immunotherapy by administering in vivo, into a tissue of a vertebrate, a Flt-3 ligand-encoding polynucleotide and one or more antigen- or cytokine-encoding polynucleotides. The polynucleotides are incorporated into the cells of the vertebrate in vivo, and a prophylactically or therapeutically effective amt. of a Flt-3 ligand and one or more antigens is produced in vivo.

IC ICM C12N015-00

CC 15-2 (Immunochemistry)
Section cross-reference(s): 3

IT Absidia
Acanthocheilonema
Acremonium
Actinomyces
Adenoviridae
Aelurostrongylus
Alphavirus
Alternaria
Ancylostoma
Angiostrongylus
Ant (Formicidae)
Aphthovirus
Ascaris
Aspergillus
Babesia
Bacillus (bacterium genus)
Bacteroides
Balantidium
Bartonella
Basidiobolus
Besnoitia
Bipolaris
Blackfly
Blastomyces
Bordetella
Borrelia
Brucella
Brugia
Bunostomum
Calicivirus
Campylobacter
Candida
Canine distemper virus
Capillaria (nematode)
Capnocytophaga
Chabertia
Chlamydia
Cimex lectularius
Clostridium
Coccidioides
Conidiobolus
Cooperia
Coronavirus
Corynebacterium
Coxiella
Crenosoma

Cryptococcus (fungus)
Cryptosporidium
Curvularia
Dermatophilus
Dictyocaulus
Dioctophyme
Dipetalonema
Diphyllobothrium
Diplopylidium
Dirofilaria
Dracunculus (worm)
Ebola virus
Ehrlichia
Eimeria
Encephalitozoon
Entamoeba
Enterobius
Enterococcus
Enterovirus
Epidermophyton
Escherichia
Exophiala
Feline infectious peritonitis virus
Filaroides
Flaviviridae
Flea (Siphonaptera)
Francisella
Fusobacterium
Geotrichum
Giardia
Gnat
Haematobia irritans
Haemobartonella
Haemonchus
Haemophilus
Hammondia
Helicobacter
Hepadnaviridae
Hepatozoon
Herpesviridae
Histoplasma
Human coxsackievirus
Human immunodeficiency virus
Human parainfluenza virus
Influenza virus
Isospora
Klebsiella
Lagochilascaris
Leishmania
Leptospira
Listeria
Loa
Louse
Madurella
Malassezia
Mansonella
Marburg virus
Microsporidia
Microsporum
Mite and Tick

Moniliella
Mortierella
Mosquito
Mucor
Muellerius
Mycobacterium
Mycoplasma
Nanophyetus
Necator
Neisseria
Nematodirus
Neorickettsia
Neospora
Nocardia
Nosema
Oesophagostomum
Onchocerca
Opisthorchis
Orthomyxovirus
Ostertagia
Paecilomyces
Papillomavirus
Parafilaria
Paragonimus
Paramyxovirus
Parascaris
Parasite
Parasitic worm
Parvovirus
Pasteurella
Penicillium
Pentatrichomonas
Peptococcus
Peptostreptococcus
Pestivirus
Phialemonium
Phialophora
Physaloptera
Picornaviridae
Plasmodium (malarial genus)
Pneumocystis
Poxviridae
Proteus (bacterium)
Protoplast and Spheroplast
Protostrongylus
Prototheca
Protozoa
Pseudallescheria
Pseudomicrodochium
Pseudomonas
Pythium
Rabies virus
Reoviridae
Respiratory syncytial virus
Retroviridae
Rhinosporidium
Rhinovirus
Rhizopus
Rickettsia
Rotavirus

Salmonella
Sandfly
Sarcocystis
Schistosoma
Scolecobasidium
Setaria (nematode)
Shigella
Spider
Spirocerca
Sporothrix
Staphylococcus
Stemphylium
Stephanofilaria
Stomoxys calcitrans
Streptococcus
Streptococcus pneumoniae
Strongyloides
Strongylus
Tabanidae
Theileria
Thelazia
Toxascaris
Toxocara
Toxoplasma
Treponema
Triatominae
Trichinella
Trichophyton
Trichosporon
Trichostrongylus
Trichuris
Trypanosoma
Tsetse fly (Glossina)
Uncinaria
Wuchereria
Xylohypha
Yersinia
(adjuvants for vector vaccines against; cDNAs encoding Flt-3 receptor **ligand** and there use as adjuvants in vector vaccines)

L16 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:98034 HCAPLUS
DOCUMENT NUMBER: 132:233229
TITLE: Bcl-2 and Bax regulate the channel activity of the mitochondrial adenine nucleotide translocator
AUTHOR(S): Brenner, Catherine; Cadiou, Herve; Vieira, Helena L. A.; Zamzami, Naoufal; Marzo, Isabel; Xie, Zhihua; Leber, Brian; Andrews, David; Duclohier, Herve; Reed, John C.; Kroemer, Guido
CORPORATE SOURCE: Centre National de la Recherche Scientifique, Villejuif, F-94801, Fr.
SOURCE: Oncogene (2000), 19(3), 329-336
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bcl-2 family proteins including anti-apoptotic (Bcl-2) or pro-apoptotic (Bax) members can form ion channels when incorporated into synthetic lipid bilayers. This contrasts with the observation that Bcl-2 stabilizes the mitochondrial membrane barrier function and inhibits the permeability

transition pore complex (PTPC). Here we provide exptl. data which may explain this apparent paradox. Bax and adenine nucleotide translocator (ANT), the most abundant inner mitochondrial membrane protein, can interact in artificial lipid bilayers to yield an efficient composite channel whose electrophysiol. properties differ quant. and qual. from the channels formed by Bax or ANT alone. The formation of this composite channel can be obsd. in conditions in which Bax protein alone has no detectable channel activity. Cooperative channel formation by Bax and ANT is stimulated by the ANT ligand atractyloside (Atr) but inhibited by ATP, indicating that it depends on the conformation of ANT. In contrast to the combination of Bax and ANT, ANT does not form active channels when incorporated into membranes with Bcl-2. Rather, ANT and Bcl-2 exhibit mutual inhibition of channel formation. Bcl-2 prevents channel formation by Atr-treated ANT and neutralizes the cooperation between Bax and ANT. Our data are compatible with a menage a trois model of mitochondrial apoptosis regulation in which ANT, the likely pore-forming protein within the PTPC, interacts with Bax or Bcl-2, with Bax and Bcl-2 dictating opposite effects on the pore-forming potential of ANT.

CC 6-3 (General Biochemistry)

ST adenine nucleotide translocator **ANT** channel activity interaction Bax Bcl2

IT Transport proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ADP/ATP carrier; Bax increases capacity of adenine nucleotide translocator **ANT** to form **atractyloside**-responsive channels, while Bcl-2 reduces channel formation by **ANT**)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Bax; Bax increases capacity of adenine nucleotide translocator **ANT** to form **atractyloside**-responsive channels, while Bcl-2 reduces channel formation by **ANT**)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(bcl-2; Bax increases capacity of adenine nucleotide translocator **ANT** to form **atractyloside**-responsive channels, while Bcl-2 reduces channel formation by **ANT**)

IT Cooperative phenomena
(cooperative channel formation by Bax and **ANT**; Bax increases capacity of adenine nucleotide translocator **ANT** to form **atractyloside**-responsive channels, while Bcl-2 reduces channel formation by **ANT**)

IT Conformation
(protein, dependence of cooperative channel formation on conformation of **ANT**; Bax increases capacity of adenine nucleotide translocator **ANT** to form **atractyloside**-responsive channels, while Bcl-2 reduces channel formation by **ANT**)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1998:725409 HCAPLUS

DOCUMENT NUMBER: 130:61252

TITLE: A single amino acid substitution in transmembrane helix VI results in overexpression of the human GnRH receptor

AUTHOR(S): Myburgh, David B.; Pawson, Adam J.; Davidson, James S.; Flanagan, Colleen A.; Millar, Robert P.; Hapgood,

Janet P.
CORPORATE SOURCE: MRC Unit for Molecular Reproductive Endocrinology, Department of Chemical Pathology, University of Cape Town Medical School, Observatory, 7925, S. Afr.
SOURCE: European Journal of Endocrinology (1998), 139(4), 438-447
CODEN: EJOEEP; ISSN: 0804-4643
PUBLISHER: BioScientifica
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Construction of constitutively active mutants of the GnRH receptor, a member of the G-protein coupled receptor superfamily, would facilitate investigation of the mechanism of receptor activation. Point mutations were introduced in the human GnRH receptor in positions corresponding to those which caused constitutive activity in other G-protein coupled receptors. The effects of these mutations on ligand binding, receptor intracellular signaling and receptor expression were detd. Wild type and mutated receptor cDNAs were expressed in COS-1 cells. Basal and agonist-stimulated inositol phosphate prodn. and ligand binding were detd. In addn., receptor mRNA levels, cell surface receptor stability and rate of internalization were measured. Although none of the mutant receptors exhibited constitutive activity, mutation of Phe-272 in transmembrane helix VI to Leu increased cell surface receptor nos., with unchanged affinities for radiolabeled agonist, superagonist and antagonist peptides compared with wild type receptor. The cell surface receptor stability and rate of internalization were similar for wild type and F272L GnRH receptors. Thus a single amino acid mutation in transmembrane helix VI causes an increase in cell surface receptor nos., which appears to result from an increased rate of receptor protein translation, processing or insertion into membranes.
CC 2-2 (Mammalian Hormones)
IT 81608-50-6, **Ant** 26 218166-79-1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(single amino acid mutation in transmembrane helix VI of GnRH receptor in relation to **ligand** binding, receptor intracellular signaling and receptor expression)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:543061 HCAPLUS
DOCUMENT NUMBER: 129:148992
TITLE: Preparation of 1-phenyl-4-benzylpiperazines as dopamine receptor subtype specific ligands (D4)
INVENTOR(S): Thurkauf, Andrew; Chen, Xi
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833784	A1	19980806	WO 1998-US1628	19980129

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
GA, GN, ML, MR, NE, SN, TD, TG

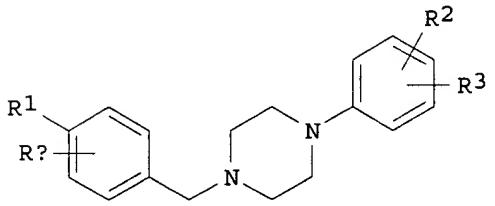
US 5859246	A	19990112	US 1997-791673	19970130	
AU 9860472	A1	19980825	AU 1998-60472	19980129	
EP 960106	A1	19991201	EP 1998-903796	19980129	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
NZ 336953	A	20010427	NZ 1998-336953	19980129	
JP 2001521492	T2	20011106	JP 1998-533030	19980129	
CN 1083448	B	20020424	CN 1998-803364	19980129	
ZA 9806876	A	20000502	ZA 1998-6876	19980731	
US 6172229	B1	20010109	US 1999-228106	19990111	
US 2002007064	A1	20020117	US 2000-736566	20001213	
US 6426347	B2	20020730			
US 2003119851	A1	20030626	US 2002-186235	20020628	

PRIORITY APPLN. INFO.:

US 1997-791673	A1	19970130
WO 1998-US1628	W	19980129
US 1999-228106	A1	19990111
US 2000-736566	A1	20001213

OTHER SOURCE(S): MARPAT 129:148992

GI



I

AB The title compds. [I; R1 = halo, C1-4 alkyl, and Ra = H; R1Ra = C3-5 alkylene contg. 1-2 oxygen atoms, benzo; R2, R3 = H, halo, C1-4 alkyl, etc.; R2R3 = C3-5 alkylene or alkenylene contg. 1-2 oxygen atoms], dopamine D4 (ant)agonists useful in the treatment of neuropsychol. diseases such as schizophrenia, psychotic depression and mania, were prepd. Thus, reaction of 1-(4-chlorophenyl)piperazine with 4-chlorobenzyl chloride in the presence of K2CO3 in MeCN afforded 56% I.2HCl [R1 = Cl; R2 = 4-Cl; R3 = Ra = H] which showed Ki of 5 nM against dopamine D4 receptor subtype binding.

IC ICM C07D295-06
ICS A61K031-495; C07D405-10

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT Dopamine receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(D4, selective (**ant**)agonists of; prepn. of 1-phenyl-4-benzylpiperazines as dopamine receptor subtype specific **ligands** (D4))

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:478668 HCAPLUS
DOCUMENT NUMBER: 127:158437
TITLE: Immobilization of cyclodextrin glucanotransferase and its reaction characteristics regarding transglucosylated stevioside production
AUTHOR(S): In, Man-Jin; Kim, Dong Chung; Chae, Hee Jeong; Choi, Kyung Seok; Kim, Min-Hong
CORPORATE SOURCE: R&D Center, Miwon Co. Ltd., Ichon, 467-810, S. Korea
SOURCE: Sanop Misaengmul Hakhoechi (1997), 25(3), 305-310
CODEN: SMHAEH; ISSN: 0257-2389
PUBLISHER: Korean Society for Applied Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB For the continuous prodn. of transglucosylated steviosides, cyclodextrin glucanotransferase from Bacillus macerans was immobilized onto Diaion HPA 75 (styrene-divinylbenzene resin) that was screened from ion exchange resins, synthetic adsorbents and chitosan derivs. The parameters influencing enzyme immobilization were examd. in order to maximize the activity of immobilized enzyme. The optimum conditions for immobilization turned out to be: contact time 2 h at 30.degree.C, pH 6.apprx.9, and enzyme loading 20 mg protein/g resin at 4.4 Os/Kg as osmolarity. Competing with other mols. having low mol. wt., the enzyme was immobilized reversibly. The activity of immobilized enzyme was as high as 180 U/g resin when the diafiltered soln. of stock enzyme was used. The optimum conditions for transglucosylation were as follows: pH 6.0, temp. 50.degree.C, 30% substrate soln. composed of 15% stevioside mixt. and 15% dextrin of which the value of dextrose equiv. was about 9.0.

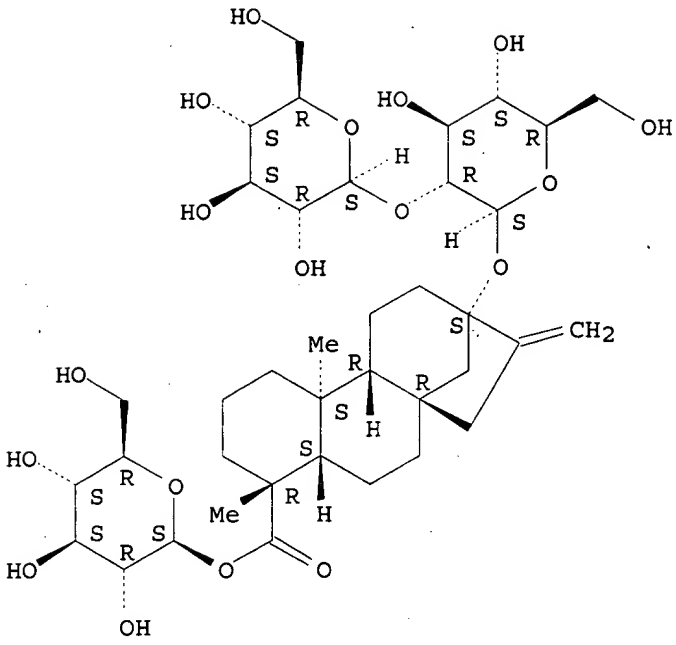
CC 7-7 (Enzymes)
Section cross-reference(s): 9, 33

IT **57817-89-7DP**, Stevioside, transglucosylated
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(**immobilization** of Bacillus macerans cyclodextrin glucanotransferase and its reaction characteristics regarding transglucosylated stevioside prodn.)

IT **57817-89-7DP**, Stevioside, transglucosylated
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(**immobilization** of Bacillus macerans cyclodextrin glucanotransferase and its reaction characteristics regarding transglucosylated stevioside prodn.)

RN 57817-89-7 HCAPLUS
CN Kaur-16-en-18-oic acid, 13-[(2-O-.beta.-D-glucopyranosyl-.beta.-D-glucopyranosyl)oxy]-, .beta.-D-glucopyranosyl ester, (4.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

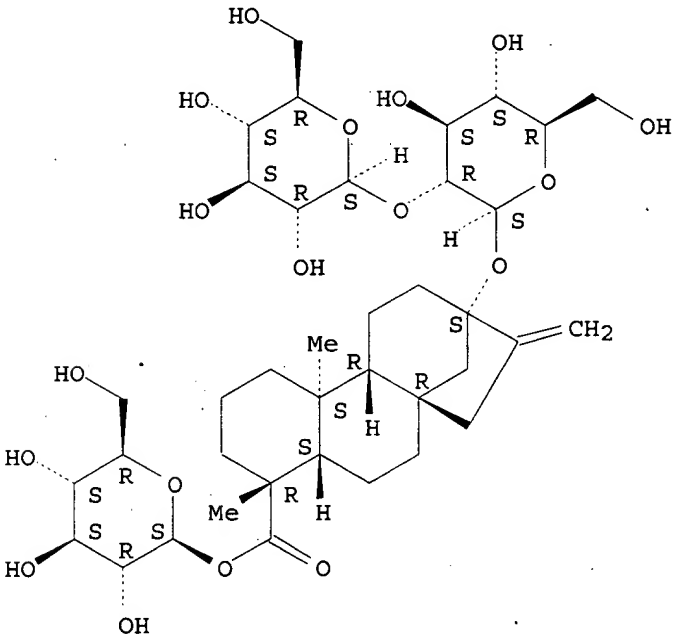


L16 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:349991 HCAPLUS
DOCUMENT NUMBER: 125:56724
TITLE: Formulation and physicochemical and rheological evaluation of low soluble solids jams with different sweeteners
AUTHOR(S): Campos, Adriane Mulinari; Candido, Lys Mary Bileski
CORPORATE SOURCE: Dep. Quim. Ind., Pontificia Univ. Catol. Parana, Brazil
SOURCE: Ciencia e Tecnologia de Alimentos (1995), 15(3), 268-278
CODEN: CTALDN; ISSN: 0101-2061
PUBLISHER: Sociedade Brasileira de Ciencia e Tecnologia de Alimentos
DOCUMENT TYPE: Journal
LANGUAGE: Portuguese

AB Low sol. solids jams with amidated pectins were prepd. with different fruits and sweeteners. They were evaluated physico-chem. and rheol. By correlation with model gels, 13 formulations of strawberry, kiwifruit, apple, and mango jams were developed. The blends of sweeteners were: sucrose/aspartame (APM), fructose/APM, glucose/APM, high maltose syrup (HMS)/APM, glucose syrup/APM, Invert sugar/APM, fructose/sorbitol/APM, mannitol/soritol/APM, APM/sorbitol, saccharin/cyclamate/sorbitol, acesulfame-K/sorbitol, stevioside/sorbitol/APM/acesulfame-K/sorbitol. Total sugars, glucose, fructose, pH, total calcium and free calcium detns. were similar to the literature. Mango jams were more consistent when compared to the medium followed by apple jams. Kiwifruit jams presented the least strength. Taking into account the blends of sweeteners, the smaller values for the penetration distance were found in APM/mannitol/sorbitol and saccharin/cyclamate/sorbitol. All jams with sugar alcs. had very similar consistency. Strawberry and kiwifruit jams presented greater variation on the gel spreadability. The sucrose jams was the least spread.

CC 17-10 (Food and Feed Chemistry)
IT 50-70-4, D-Glucitol, biological studies 57-50-1, biological studies 69-65-8, Mannitol 81-07-2 100-88-9, Cyclamate 8013-17-0, Invert sugar 22839-47-0, Aspartame 33665-90-6, Acesulfame 55589-62-3, Acesulfame potassium **57817-89-7**, Stevioside
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(formulation and physicochem. and rheol. evaluation of low sol. **solids** jams with different sweeteners)
IT **57817-89-7**, Stevioside
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(formulation and physicochem. and rheol. evaluation of low sol. **solids** jams with different sweeteners)
RN 57817-89-7 HCAPLUS
CN Kaur-16-en-18-oic acid, 13-[(2-O-.beta.-D-glucopyranosyl-.beta.-D-glucopyranosyl)oxy]-, .beta.-D-glucopyranosyl ester, (4.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:471308 HCAPLUS
DOCUMENT NUMBER: 119:71308
TITLE: Solid delivery systems for hydrophobic liquids
INVENTOR(S): Fuisz, Richard C.
PATENT ASSIGNEE(S): Fuisz Technologies Ltd., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9308699	A1	19930513	WO 1992-US9447	19921030
W: AU, BR, CA, CS, FI, HU, JP, KR, NO, PL, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
WO 9107952	A1	19910613	WO 1990-US6093	19901024
W: AU, BR, HU, JP, KR, SU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9066488	A1	19910626	AU 1990-66488	19901024
AU 640966	B2	19930909		
EP 502865	A1	19920916	EP 1990-916659	19901024
EP 502865	B1	19950906		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
BR 9007887	A	19920929	BR 1990-7887	19901024
JP 2972335	B2	19991108	JP 1990-515637	19901024
IL 96199	A1	19941128	IL 1990-96199	19901031
CA 2029175	AA	19910531	CA 1990-2029175	19901101
CA 2029175	C	19960521		
ZA 9009092	A	19910925	ZA 1990-9092	19901113
CA 2099493	AA	19930505	CA 1992-2099493	19921030
AU 9230630	A1	19930607	AU 1992-30630	19921030
AU 661081	B2	19950713		
EP 565706	A1	19931020	EP 1992-924248	19921030
EP 565706	B1	19970129		
R: BE, CH, DE, FR, GB, IE, IT, LI, LU, NL				
JP 06504448	T2	19940526	JP 1992-508683	19921030
PL 171158	B1	19970328	PL 1992-300040	19921030
US 5370881	A	19941206	US 1993-81338	19930629
CA 2141909	AA	19950811	CA 1995-2141909	19950206
EP 667147	A2	19950816	EP 1995-650004	19950208
EP 667147	A3	19960424		
R: BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE				
JP 08038138	A2	19960213	JP 1995-43651	19950209
CN 1119934	A	19960410	CN 1995-102933	19950210

PRIORITY APPLN. INFO.:		
US 1991-787245	A2	19911104
US 1987-40371	B2	19870420
US 1988-169838	A2	19880318
US 1988-283742	A3	19881213
US 1989-444045	A	19891130
US 1990-602485	A2	19901024
WO 1990-US6093	A	19901024
WO 1992-US9447	A	19921030
US 1994-194682	A	19940210

AB The solid delivery systems for rapid release of hydrophobic liqs. comprise a water-sol., flash-flow formed matrix contg. a micronized dispersion of a substantially hydrophobic liq. such as a flavor oil. The flash-flow formed matrix can be further reduced to finer particles by pulverizing, grinding such as cryogrinding, or sieving. The solid delivery system is used in food such as chewing gum, cosmetic, dentifrice, etc.

IC ICM A23G003-30
ICS A23L001-222; A23P001-04

CC 17-14 (Food and Feed Chemistry)
Section cross-reference(s): 62

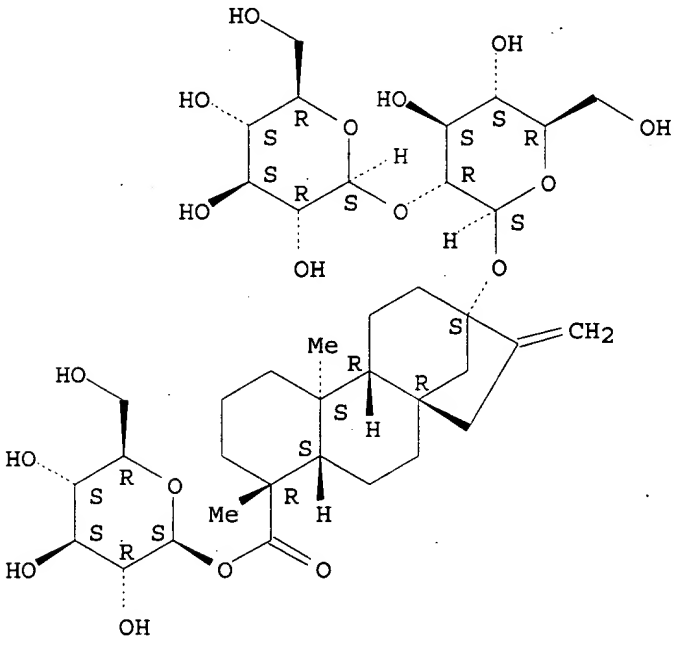
IT 81-07-2 81-07-2D, salts 100-88-9D, Cyclamate, salts 1083-30-3, Dihydrochalcone 33665-90-6, Acesulfame 33665-90-6D, Acesulfame, salts **57817-89-7**
RL: BIOL (Biological study)

(in flash-flow formed matrix, for prepn. of **solid** delivery system for hydrophobic liqs.)

IT **57817-89-7**
RL: BIOL (Biological study)
(in flash-flow formed matrix, for prepn. of **solid** delivery system for hydrophobic liqs.)

RN 57817-89-7 HCAPLUS
CN Kaur-16-en-18-oic acid, 13-[(2-O-.beta.-D-glucopyranosyl-.beta.-D-glucopyranosyl)oxy]-, .beta.-D-glucopyranosyl ester, (4.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L18 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:696159 HCAPLUS
DOCUMENT NUMBER: 137:246071
TITLE: Gene expression profiles relating to normal and osteoarthritic cartilage
INVENTOR(S): Liew, Choong-Chin; Marshall, Wayne E.; Zhang, Hongwei
PATENT ASSIGNEE(S): Chondrogene Inc., Can.
SOURCE: PCT Int. Appl., 777 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070737	A2	20020912	WO 2002-CA247	20020228
WO 2002070737	C1	20021031		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-271955P P 20010228
US 2001-275017P P 20010312
US 2001-305340P P 20010713

AB The invention provides gene expression profiles comprising one or more polynucleotide sequences that are expressed in chondrocytes from any of the following developmental and disease stages: fetus, normal adult, mild osteoarthritis, moderate osteoarthritis, marked osteoarthritis, and severe osteoarthritis. Complementary DNA libraries were constructed from human fetal, normal, mild osteoarthritic and severe osteoarthritic cartilage samples (13,398, 17,151, 12,651, and 14,222 expressed sequence tags (ESTs), resp.). The known and novel clones derived from these libraries were then used to construct human chondrocyte-specific microarrays to generate differential gene expression profiles useful as a diagnostic tools for detection of osteoarthritis. A total of 5807 expressed gene sequences are provided and matched to known gene sequences, other ESTs, or mitochondrial, ribosomal, vector, and cDNA/hypothetical protein sequences in the public databases. Arrays of the invention are useful as a gold std. for osteoarthritis diagnosis and for use to identify and monitor therapeutic efficacy of new drug targets.

IC ICM C12Q001-68

CC 14-11 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 3, 9, 63

IT 389182-82-5, DNA (human clone pcD51 cDNA) 389182-84-7, GenBank M22636 389182-85-8, DNA (human gene PSAP cDNA) 389182-94-9 389183-38-4, DNA (human cell line U937 cDNA) 389184-05-8 389184-06-9, DNA (human melanoma protein nck cDNA) 389184-15-0 389184-17-2, DNA (human cell line 184N cDNA) 389184-39-8, DNA (human gene CD59) 389184-63-8 389184-66-1, DNA (human clone cAPOD.[6,8,16] cDNA) 389184-91-2, DNA (human gene ETFA cDNA) 389185-06-2, GenBank X07290 389185-07-3, GenBank X03473 389185-34-6, DNA (human gene MYCL2) 389185-38-0, DNA (human gene OAT) 389185-41-5 389185-45-9 389185-47-1 389186-25-8, DNA (human gene PF4 cDNA) 389186-29-2 389186-73-6, DNA (human gene MACS cDNA) 389186-75-8 389186-77-0 389186-78-1 389186-95-2, GenBank X13923 389187-16-0, GenBank J00200 389187-24-0 389187-63-7, DNA (human cell line U937 cDNA) 389189-08-6, DNA (human gene SPTAN1 cDNA) 389189-14-4 389189-26-8 389189-34-8, DNA (human clone pGC1853 gene KRT18) 389189-61-1, GenBank M31013 389189-62-2, GenBank M25160 389189-78-0, GenBank M33764 389190-12-9, DNA (human tenascin cDNA plus flanks) 389190-62-9 389190-63-0, DNA (Oryctolagus cuniculus cDNA) 389190-65-2, GenBank M19503 389190-72-1, DNA (human cyclin cDNA) 389190-97-0, DNA (human gene DMD cDNA) 389191-18-8 389191-27-9 389192-52-3 389195-33-9 389195-41-9 389196-96-7 389200-21-9

389200-23-1, DNA (human cell line HeLa gene RCC1) 389200-44-6
389202-86-2, DNA (human cell line CRL-1262 cDNA) 389203-07-0
389207-09-4 389207-77-6 389210-25-7, DNA (human gene HO57 cDNA)
389210-72-4 389211-78-3 389212-46-8 389217-81-6, DNA (human gene
MFAP2 cDNA) 389231-41-8 389231-42-9, DNA (human clone cosmid 4.10)
389239-82-1, DNA (human cell line Hela gene TRIP9) 389267-28-1
389278-86-8 389278-88-0, DNA (human gene CHRM3 plus flanks)
389307-99-7, DNA (human clone GT218 gene PRL-1 cDNA) 389308-04-7
389310-16-1 389312-68-9 389324-25-8, DNA (human cell line HL60 cDNA)
389324-96-3, DNA (human clone I-14 cDNA) 389330-22-7 389334-76-3
389346-05-8 389348-91-8, DNA (human gene **ANT**-2) 389350-71-4
389357-20-4, DNA (human osteonidogen cDNA) 389357-94-2 389365-02-0
389386-88-3 389397-11-9 389398-07-6 389398-09-8 389398-33-8
389399-94-4 389411-22-7 389419-32-3 389426-48-6, DNA (human clone
GS3760 cDNA) 389444-75-1 389450-55-9, DNA (human gene POH1 cDNA)
389451-22-3, DNA (human clone cosmid IIIA9) 389475-49-4, DNA (human
gene NHC cDNA) 389494-64-8 389713-15-9 389728-33-0, DNA (human gene
HP cDNA) 389730-81-8 389731-50-4 389732-09-6 389751-37-5
389752-19-6 389753-88-2, DNA (human clone 23819 gene white cDNA)
389767-38-8 389775-70-6 389775-85-3, DNA (human gene HDIA1 cDNA)
389776-72-1 389781-65-1 389782-56-3 389786-46-3 389791-74-6, DNA
(human ARE1-like protein cDNA) 389793-67-3 389793-69-5 389794-86-9
390055-04-6 390055-05-7 390055-06-8 390069-21-3 390075-18-0
390080-36-1 390087-08-8, GenBank AJ012078 390096-57-8 390105-83-6,
GenBank AF109907 390105-90-5 390107-84-3, DNA (human gene SVIL cDNA)
390108-81-3, DNA (human fumarase cDNA plus flanks) 390108-93-7
390109-00-9 390111-00-9 390111-44-1 390116-03-7 390117-38-1
390117-42-7 390117-51-8 390117-52-9 390117-55-2, DNA (human gene
IPP-2 cDNA) 390118-40-8 390119-08-1 390119-28-5, GenBank AF110824
390119-29-6 390119-31-0 390119-38-7 390119-54-7 390119-61-6
390120-46-4 390121-41-2, GenBank AF092136 390121-43-4 390121-44-5,
GenBank AF100742 390123-00-9, DNA (human gene RGS5 cDNA) 390124-92-2,
GenBank AF155111 390124-93-3, GenBank AF155113 390124-94-4, GenBank
AF155114 390125-34-5, GenBank AF106684 390126-04-2 390139-16-9
390141-06-7, DNA (human UMP-CMP kinase cDNA) 390165-84-1 390173-07-6
390187-72-1, GenBank M15887 390188-25-7 390189-32-9 390189-74-9
390190-30-4, DNA (human gene APC7 cDNA) 390199-59-4, DNA (human gene
HGRG8 cDNA) 390216-54-3 390219-99-5, DNA (human gene MASA cDNA)
390220-01-6 390221-78-0 390221-80-4, DNA (human MEK binding partner 1
cDNA) 390227-73-3, DNA (human gene IFI16b) 390232-05-0, DNA (human
gene ADAMTS1 cDNA) 390234-35-2, DNA (human gene YEAF1 cDNA)
390240-22-9, DNA (human clone CBFBBF03 HSPC299 cDNA) 390240-24-1, DNA
(human clone CBFBQE02 HSPC307 cDNA) 390240-25-2, DNA (human clone
CBLABB10 HSPC310 cDNA) 390240-27-4, DNA (human clone CBNBDE02 HSPC337
cDNA) 390241-86-8 390244-98-1, DNA (human gene NFKB1) 390254-72-5
390257-79-1, DNA (human clone PLACE1007725 cDNA) 390259-38-8, DNA (human
PDNP1 gene) 390259-39-9, DNA (human gene HEI10 cDNA) 390267-04-6, DNA
(human gene HT015 cDNA) 390293-42-2 390293-84-2, DNA (human gene
RARG-1 cDNA) 390293-89-7 390330-43-5, DNA (human clone PLACE1011646
cDNA) 390632-71-0, DNA (human clone PLACE1008398 cDNA) 391522-25-1
391523-78-7 391523-86-7, GenBank M58485 391524-00-8, DNA (human gene
PPIB cDNA) 391524-68-8, DNA (human gene PI cDNA) 391524-83-7
391525-01-2 391525-16-9, GenBank J03799 391525-32-9 391525-60-3, DNA
(human cell line HL-60 cDNA) 391525-61-4 391525-63-6, DNA (human gene
MPP1 cDNA) 391525-64-7, DNA (human gamma-actin cDNA) 391525-65-8
391525-71-6 391525-72-7, GenBank X54304 391525-76-1 391525-77-2
391525-78-3 391526-01-5 391526-06-0 391526-21-9, GenBank V00710
391526-23-1 391526-46-8, DNA (human cDNA) 391526-56-0, DNA (human
cDNA) 391526-58-2, DNA (human gene HF cDNA) 391526-67-3 391526-70-8,
GenBank X03558 391526-75-3, DNA (human gene ERCC3 protein cDNA)

391526-82-2, DNA (human cell line FS-2 cDNA) 391526-88-8 391527-15-4
391527-17-6, GenBank M21389 391527-19-8, DNA (human gene G22P1)
391527-20-1 391527-30-3, DNA (human gene LYZ cDNA) 391527-39-2, DNA
(human clone Op-30 cDNA) 391527-41-6, DNA (human gene LAP18 cDNA)
391527-45-0 391527-56-3, DNA (human gelsolin cDNA plus flanks)
391527-72-3 391527-73-4 391527-77-8 391527-87-0 391527-88-1,
GenBank X04588 391527-91-6, DNA (human gene .beta.2 plus flanks)
391527-93-8, DNA (human gene VIL2 cDNA) 391528-06-6 391528-16-8
391528-20-4, DNA (human gene FAH cDNA)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(nucleotide sequence; gene expression profiles relating to normal and
osteoarthritic cartilage)

IT 391995-05-4 391995-61-2 391996-11-5, DNA (human tyrosyl-tRNA
synthetase cDNA) 391998-11-1 392007-93-1 392010-84-3 392011-04-0
392011-08-4 392012-20-3 392012-21-4, DNA (human DEC1 cDNA)
392013-07-9 392013-11-5 392013-29-5, GenBank AF000160 392013-36-4
392013-48-8 392013-54-6, GenBank AF001893 392013-60-4 392013-68-2,
DNA (human gene SKB1Hs cDNA) 392015-08-6 392015-11-1 392015-14-4
392015-70-2 392015-75-7 392016-23-8 392016-31-8 392016-36-3
392017-92-4 392018-07-4, DNA (human gene MGST3 cDNA) 392019-60-2
392019-68-0 392019-69-1 392019-74-8 392019-82-8 392020-02-9, DNA
(human gene PPT exon 9 plus flanks) 392020-03-0 392020-34-7
392020-51-8 392021-37-3, DNA (human TRAF5 cDNA) 392021-43-1, DNA
(human gene ABC50 cDNA) 392022-63-8 392022-69-4, GenBank AF022861
392024-15-6 392024-19-0 392024-53-2 392024-65-6 392024-74-7, DNA
(human gene DBX) 392025-08-0 392025-30-8 392025-31-9 392025-45-5,
DNA (human gene CYR61 cDNA) 392026-10-7, DNA (human clone 2-1 cDNA)
392026-11-8 392026-18-5 392027-07-5, GenBank AF080092 392027-21-3
392027-24-6 392027-39-3 392027-42-8 392027-44-0 392027-47-3
392027-48-4 392027-49-5 392027-50-8 392027-52-0 392027-53-1
392027-56-4, DNA (human clone hh03913 cDNA) 392027-65-5 392027-69-9
392027-70-2 392027-74-6 392027-80-4 392029-60-6 392029-62-8
392029-64-0 392029-66-2, DNA (human clone HG1339 gene KIAA0407)
392029-67-3 392029-68-4 392029-81-1, GenBank AF000367 392029-84-4
392029-93-5, DNA (human clone HG0960) 392029-94-6, DNA (human clone
HG0965 cDNA) 392029-95-7, DNA (human clone HH0916) 392030-07-8
392031-98-0 392032-26-7 392036-89-4 392037-04-6 392037-14-8
392037-24-0 392037-26-2, DNA (human gene RZF cDNA) 392038-10-7
392038-27-6 392038-31-2, DNA (human gene NID-2 cDNA) 392038-46-9
392038-96-9, DNA (mouse strain 129SVJ ADAMTS-1 gene) 392038-97-0
392039-05-3 392039-46-2 392039-68-8 392039-73-5 392039-86-0, DNA
(human gene BARD1 exons 10-11) 392042-00-1 392042-74-9 392043-21-9
392043-28-6 392043-29-7 392043-35-5 392043-70-8 392043-81-1
392044-64-3, DNA (human gene PDZK1 cDNA) 392047-15-3 392047-42-6
392048-67-8 392048-69-0 392048-75-8 392048-91-8 392049-34-2
392049-35-3 392049-44-4 392049-62-6, DNA (human gene CTNS cDNA)
392049-76-2, DNA (human gene GRY-RBP cDNA) 392049-78-4, DNA (human
perilipin cDNA) 392049-83-1 392049-85-3 392049-87-5 392049-90-0
392049-91-1 392049-92-2 392049-93-3 392049-97-7 392050-05-4
392050-06-5 392050-13-4 392050-17-8 392050-19-0 392050-20-3
392050-21-4 392050-25-8 392050-27-0 392050-29-2 392050-30-5
392050-31-6 392050-34-9 392050-38-3 392050-42-9 392050-47-4
392050-51-0, DNA (human gene Kin17 cDNA) 392050-67-8 392050-80-5, DNA
(human osteoprotegerin **ligand** cDNA) 392050-89-4 392051-76-2
392051-77-3 392052-15-2, DNA (human gene Sab cDNA) 392052-34-5, DNA
(human gene UGDH cDNA) 392052-71-0 392053-54-2 392053-56-4
392053-68-8 392053-80-4 392054-10-3 392054-16-9 392054-58-9
392055-57-1 392055-93-5, GenBank AC005005 392057-36-2 392057-48-6,
DNA (human geminin cDNA plus flanks) 392057-62-4, DNA (human cell line

ZR-75 gene SP100) 392057-71-5 392057-76-0 392057-94-2, GenBank AF055066 392058-01-4 392058-17-2 392058-18-3, GenBank AC005210 392058-26-3, DNA (human gene PACT cDNA) 392058-28-5 392058-41-2, DNA (human GRP1 protein cDNA) 392058-45-6, DNA (human .beta.-filamin cDNA plus flanks) 392058-48-9 392058-75-2, DNA (human gene tom1 cDNA) 392058-80-9 392058-82-1 392058-85-4 392058-86-5 392058-89-8 392058-91-2 392058-92-3 392058-93-4 392058-97-8 392058-98-9 392059-00-6 392059-02-8, DNA (human clone HK02346 gene KIAA0669) 392059-04-0 392059-10-8 392059-11-9 392059-19-7 392059-22-2 392059-23-3 392059-24-4 392059-39-1 392059-43-7 392059-48-2 392059-59-5 392059-60-8, DNA (human G protein .gamma.5-subunit cDNA) 392059-62-0 392059-63-1 392059-65-3, GenBank AF038960 392059-73-3, DNA (human NORI-1 cDNA) 392059-79-9, DNA (human histone macroH2A1.2 cDNA) 392059-89-1 392060-50-3, GenBank AF049672 392060-73-0 392060-81-0, DNA (human gene CLECSF1 exon 3) 392060-83-2 392060-89-8 392060-92-3 392061-01-7 392061-19-7, DNA (human gene MRJ cDNA) 392061-59-5, GenBank AF081192 392061-60-8, DNA (human .alpha.-tubulin isoform 1 cDNA) 392062-15-6 392064-08-3 392064-09-4 392064-32-3 392064-79-8 392064-89-0 392065-00-8 392065-08-6 392065-09-7 392065-11-1 392065-12-2 392065-13-3 392065-14-4 392065-16-6, DNA (human clone hk04073s1 cDNA) 392065-17-7 392065-23-5 392065-26-8 392065-30-4 392065-34-8
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; gene expression profiles relating to normal and osteoarthritic cartilage)

L18 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:359465 HCAPLUS
DOCUMENT NUMBER: 137:194459
TITLE: Synthesis, characterisation and crystal structure of cis-dioxomolybdenum(VI) complexes of some potentially pentadentate but functionally tridentate (ONS) donor **ligands**
AUTHOR(S): Rana, Arindam; Dinda, Rupam; Sengupta, Parbati; Ghosh, Saktiprosad; Falvello, Larry R.
CORPORATE SOURCE: Department of Inorganic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata, 700 032, India
SOURCE: Polyhedron (2002), 21(9-10), 1023-1030
CODEN: PLYHDE; ISSN: 0277-5387
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:194459
AB Neutral cis-dioxomolybdenum(VI) complexes with potentially pentadentate ONSNO donor Schiff bases of thiocarbodihydrazone of salicylaldehyde (H3L1), 5-bromosalicyladehyde (H3L2), 5-nitrosalicylaldehyde (H3L3) and 2-hydroxyacetonphenone (H3L4) acting as tridentate ONS donor ligands were synthesized. The complexes are MoO2LH(R-OH) (R = CH3) where, LH = L1H, L2H, L3H and L4H. The complexes were characterized by elemental analyses, UV, IR, and 1H NMR spectroscopy, magnetic susceptibility measurement, molar conductivities in soln. and by cyclic voltammetry. Two of [MoO2(L2H)(MeOH)] and [MoO2(L4H)(MeOH)] were crystallog. characterized. The structures reveal that the Mo acceptor center is present in a distorted octahedral NO4S donor environment. The presence of a substituent either on the arom. ring of the salicylaldehyde moiety or on the C atom of its carbonyl group is found to exhibit little effect on the corresponding metal ligand bond distances and angles. The 6th coordination site of the complexes harboring the weakly coordinated R-OH

moiety is found to act as the binding site for various neutral monodentate Lewis bases.

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 72, 75

IT Reduction, electrochemical
Reduction potential
(of salicylaldehyde/hydroxyacetophenone thiocarbodihydrazones and their molybdenum oxo complexes)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:66860 HCAPLUS
DOCUMENT NUMBER: 136:130775
TITLE: Sequencing, characterization and use of caspase-14 from human and mouse
INVENTOR(S): Alnemri, Emad S.; Fernandez-Alnemri, Teresa
PATENT ASSIGNEE(S): Thomas Jefferson University, USA
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 139,600.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6340740	B1	20020122	US 1998-187789	19981106
US 6432628	B1	20020813	US 1998-139600	19980825
WO 2000028047	A1	20000518	WO 1999-US25523	19991029
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1124971	A1	20010822	EP 1999-971856	19991029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002534958	T2	20021022	JP 2000-581214	19991029
US 2002146804	A1	20021010	US 2001-989903	20011120
US 2003040096	A1	20030227	US 2002-68564	20020205

PRIORITY APPLN. INFO.:

US 1997-56986P	P	19970826
US 1998-139600	A2	19980825
US 1998-187789	A	19981106
WO 1999-US25523	W	19991029
US 2001-989903	A1	20011120

AB The invention provides an isolated nucleic acid mol. encoding the human and mouse apoptotic caspase-14 polypeptide or functional fragment thereof, an expression vector that contains the nucleic acid mol. and a host cell that contains the vector. The gene or nucleic acid mol. can include single or double stranded nucleic acids corresponding to coding or non-coding strands of the caspase-14 nucleotide sequence. The cDNA and amino acid sequences of mouse and human caspase-14 precursor and splicing variants are provided, along with the cleavage sites used in the formation of large and small subunits. The invention also provides for antibodies that specifically bind to human and mouse caspase-14, and methods of

identifying compds. that modulate caspase-14 activity. Similar to other caspases, caspase-14 is produced as a proenzyme, which is proteolytically cleaved into two subunits, which assoc. and form the functional enzyme. Mouse caspase-14 was shown to be processed by granzyme B, caspase 10 and caspase 8, but not with other caspases. In addn., the invention relates to methods of identifying compds. that modulate caspase-14 activity. No cleavage/activation of procaspase-14 was obsd. in cytochrome c and dATP activated S100 exts.

IC ICM C07K001-00
ICS C07K014-00; C12N009-00; C12P021-04
NCL 530350000
CC 7-5 (Enzymes)
Section cross-reference(s): 3, 13
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study) (TRAIL (tumor necrosis factor-related apoptosis-inducing **ligand**), procaspase-14 processing by; sequencing, characterization and use of caspase-14 from human and mouse)
IT Fas antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**ant**-Fas antibodies, procaspase-14 processing by; sequencing, characterization and use of caspase-14 from human and mouse)
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:676911 HCAPLUS
DOCUMENT NUMBER: 135:238598
TITLE: Cloning, sequence and therapeutic applications of human sphingomyelinase isoenzymes
INVENTOR(S): Amtmann, Eberhard; Chlichlia, Katherini
PATENT ASSIGNEE(S): Deutsches Krebsforschungszentrum, Germany; Denison, Christopher Marcus
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066709	A2	20010913	WO 2001-GB998	20010306
WO 2001066709	A3	20020516		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1265991	A2	20021218	EP 2001-910008	20010306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: GB 2000-5326 A 20000306
WO 2001-GB998 W 20010306
OTHER SOURCE(S): MARPAT 135:238598
AB Two novel human sphingomyelinases are provided, having optimum activities

at pH 7 and pH 8, resp. The two proteins have different tissue sources, the pH 7 form from T-cell lymphomas, and the pH 8 form from B-cell lymphomas. Cloning, expression and cDNA sequence of the pH 7 sphingomyelinase isoenzyme are reported. Sensitivity of the pH 7 isoenzyme to sphingomyelinase inhibitor C11AG has been detd. Stimulation of apoptosis in human T-cell lymphoma cells by C11AG has been reported. Methods of treatment and diagnosis, fragments, antibodies, nucleic acids and pharmaceutical compns. are also provided.

IC ICM C12N009-16
ICS C12N015-55; C07K016-40; A61K038-17; C12Q001-34; G01N033-68

CC 7-2 (Enzymes)
Section cross-reference(s): 1, 3, 13, 63

IT Fas antigen
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**ant**-CD95 antibody; cloning, sequence and therapeutic applications of human sphingomyelinase isoenzymes)

IT Apoptosis
(inducing CD95-**ligand**/fas-mediated apoptosis; cloning, sequence and therapeutic applications of human sphingomyelinase isoenzymes)

IT Fas **ligand**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(inducing CD95-**ligand**/fas-mediated apoptosis; cloning, sequence and therapeutic applications of human sphingomyelinase isoenzymes)

L18 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:685117 HCAPLUS
DOCUMENT NUMBER: 129:314987
TITLE: Canine Fc epsilon receptor and allergen to detect canine IgE
INVENTOR(S): Frank, Glenn Robert; Rushlow, Keith E.
PATENT ASSIGNEE(S): Heska Corporation, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9845707	A1	19981015	WO 1998-US6774	19980406
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6060326	A	20000509	US 1997-833488	19970407
AU 9867964	A1	19981030	AU 1998-67964	19980406
PRIORITY APPLN. INFO.:			US 1997-833488	19970407
			WO 1998-US6774	19980406

AB The present invention includes a method to detect canine IgE using a canine Fc epsilon receptor (Fc.epsilon.R) to detect canine IgE antibodies in a biol. sample from a canine. A method comprises contacting immobilized allergen with sample to form allergen-IgE complexes, followed

by contacting with immobilized Fc.epsilon.R for quantitating IgE and for diagnosing allergy. The allergen is derived from fungi, trees, weeds, shrubs, grasses, wheat, corn, soybean, rice, eggs, milk, cheese, bovine, poultry, swine, sheep, yeast, fleas, flies, mosquitos, mites, midges, biting gnats, lice, bees, wasps, ants, true bugs and ticks. The present invention also relates to kits to perform such methods.

IC ICM G01N033-566
ICS G01N033-68

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3

IT **Ant** (Formicidae)
Bee
Cattle
Cheese
Chironomidae
Corn
Egg, poultry
Flea (Siphonaptera)
Fly (Diptera)
Fungi
Gnat
Grass (Poaceae)
Louse
Milk
Mite and Tick
Mosquito
Poultry
Rice (Oryza sativa)
Sheep
Soybean (Glycine max)
Swine
Tree
Wasp
Weed
Wheat
Yeast
(allergen; canine Fc epsilon receptor and allergen to detect canine IgE)

IT **Ligands**
Radionuclides, biological studies
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(canine Fc epsilon receptor and allergen to detect canine IgE)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:388688 HCAPLUS
DOCUMENT NUMBER: 129:66836
TITLE: Method to detect IgE
INVENTOR(S): Frank, Robert Glenn; Porter, James P.; Rushlow, Keith E.; Wassom, Donald L.
PATENT ASSIGNEE(S): Heska Corporation, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9823964	A1	19980604	WO 1997-US21651	19971124
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5945294	A	19990831	US 1996-756387	19961126
AU 9874114	A1	19980622	AU 1998-74114	19971124
EP 943097	A1	19990922	EP 1997-949625	19971124
EP 943097	B1	20030730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001507792	T2	20010612	JP 1998-526731	19971124
US 6309832	B1	20011030	US 1999-285873	19990331
US 2002034771	A1	20020321	US 2001-944277	20010830

PRIORITY APPLN. INFO.:	US 1996-756387	A	19961126
	WO 1997-US21651	W	19971124
	US 1999-285873	A3	19990331

AB The present invention includes a method to detect IgE using a human Fc epsilon receptor (Fc.epsilon.R) to detect IgE antibodies in a biol. sample from a cat, a dog, or a horse. The present invention also relates to kits to perform such methods. The kits comprise an allergen common to all regions of the United States and a human Fc.epsilon. receptor mol.

IC ICM G01N033-68
ICS G01N033-566

CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 9

IT Agrostis alba
Alternaria
Alternaria alternata
Ant (Formicidae)
Ash (Fraxinus)
Ash (Fraxinus pennsylvanica)
Aspergillus
Aspergillus fumigatus
Aureobasidium pullulans
Bee
Bermuda grass
Birch (Betula)
Blattaria
Bromus
Cattle
Cedar
Cheese
Chironomidae
Cladosporium
Cladosporium herbarum
Corn
Dermatophagoides
Dermatophagoides farinae
Dirofilaria immitis
Egg, poultry
Elm (Ulmus)
Elm (Ulmus americana)
Fescue (Festuca elatior)

Fly (Diptera)
Fungi
Fusarium
Fusarium vasinfectum
Gnat
Grass (Poaceae)
Hamelia patens
Helminthosporium
Helminthosporium sativum
Johnson grass (Sorghum halepense)
Kentucky bluegrass (Poa pratensis)
Lamb's-quarter
Lolium perenne
Louse
Maple (Acer negundo)
Mite and Tick
Mosquito
Mucor
Mucor racemosus
Mulberry
Oak (Quercus)
Oak (Quercus rubra)
Orchard grass
Penicillium
Penicillium notatum
Pigweed
Plane tree (Platanus)
Plant (Embryophyta)
Plantago lanceolata
Poplar (Populus)
Poultry
Pullularia
Ragweed (Ambrosia)
Ragweed (Ambrosia artemisiifolia)
Rhizopus
Rhizopus stolonifer
Rice (Oryza sativa)
Rumex crispus
Sage (Salvia)
Sheep
Soybean (Glycine max)
Swine
Timothy (Phleum pratense)
Tree
Trichophyton
Walnut
Walnut (Juglans nigra)
Wasp
Weed
Wheat
Xanthium
Yeast
(allergen; test kit comprising allergen and human Fc.epsilon.R for detecting IgE)

IT Agglutinins and Lectins
Avidins
Ligands
Radionuclides, biological studies
Reagents
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(test kit comprising allergen and human Fc.epsilon.R for detecting IgE)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:509400 HCAPLUS
DOCUMENT NUMBER: 113:109400
TITLE: Studies on histaminergic compounds. Part VII. Histamine H2-binding on guinea pig cerebral cortex compared to histamine (**ant**)agonism
AUTHOR(S): Sterk, G. J.; Kramer, K.; Van der Goot, H.; Timmerman, H.
CORPORATE SOURCE: Dep. Pharmacochem., Vrige Univ., Amsterdam, 1081 HV, Neth.
SOURCE: Journal of Receptor Research (1989), 9(6), 417-27
CODEN: JRERDM; ISSN: 0197-5110
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pKD values of series of H2-active compds., obtained from displacement curves of [3H]tiotidine from a guinea-pig cerebral cortex homogenate were compared with the pA2/pD2 values of these compds. on the right atrium of the same animal species. A good correlation was found between the cortex pKD value and the pharmacol. activity of the right atrium, esp. with the antagonists, the partial agonists and the agonistic impromidine analogs (guanidines). The poor correlation between cortex pKD and atrium pD2 of some other agonists (the amines)might be explained by the presence of spare receptors for these compds. The different no. of spare receptors for the guanidines and the amines might be explained by the differences in base strength of these compds.
CC 2-2 (Mammalian Hormones)
IT Receptors
RL: BIOL (Biological study)
(histaminic H2, **ligands** binding by, in cerebral cortex, spare receptor concept on structure in relation to)

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=> d his

     (FILE 'WPIDS' ENTERED AT 10:38:32 ON 18 AUG 2003)
                DEL HIS Y
L1           3432 S ANT OR ADENINE NUCLEOTID? TRANSLOC?
L2              9 S ATRACTYLOSID?
L3              4 S L1 (L) L2
L4             92 S L1 (S) LIGAND?
L5             10 S ?ATRACTYLOSI?
L6              5 S L5 AND L1
L7              5 S L3 OR L6
L8             35 S L1 (5A) LIGAND?
L9              0 S L8 AND (D16 OR S03)/DV
L10            31 S L8 AND (D16 OR S03)/DC
L11             0 S L10 AND D04/DC
L12            31 S L10 AND B04/DC
L13            29 S L12 NOT L7
L14             8 S L13 AND (FLURO? OR LABEL? OR RADIO? OR EU3# OR EU  OR EUROP?)

=> d .wp l7 1-5;d .wp l14 1-8

L7   ANSWER 1 OF 5  WPIDS  COPYRIGHT 2003 THOMSON DERWENT on STN
AN   2002-383045 [41]   WPIDS
DNC  C2002-107929
TI   Preventing human immunodeficiency virus-1 viral protein R-adenine
     nucleotide translocator interaction, useful to prevent
     channel formation in mitochondrial membranes.
DC   B04 D16
IN   BELZACQ, A; BRENNER-JAN, C; EDELMAN, L; HOEBEKE, J; JACOTOT, E D F;
     KROEMER, G; ROQUES, B P; EDELMANN, L
PA   (BELZ-I) BELZACQ A; (BREN-I) BRENNER-JAN C; (EDEL-I) EDELMAN L; (HOEB-I)
     HOEBEKE J; (JACO-I) JACOTOT E D F; (KROE-I) KROEMER G; (ROQU-I) ROQUES B
     P; (CNRS) CENT NAT RECH SCI; (INRM) INSERM INST NAT SANTE & RECH MEDICALE;
     (INSP) INST PASTEUR; (UYCO-N) UNIV COMPIEGNE
CYC  96
PI   WO 2002020570 A2 20020314 (200241)* EN   65p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
            LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU
            SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
     US 2002068273 A1 20020606 (200241)
     AU 2002015004 A  20020322 (200251)
ADT  WO 2002020570 A2 WO 2001-EP11316 20010911; US 2002068273 A1 Provisional US
     2000-231539P 20000911, Provisional US 2000-232841P 20000915, US
     2001-949650 20010912; AU 2002015004 A AU 2002-15004 20010911
FDT  AU 2002015004 A Based on WO 200220570
PRAI US 2000-232841P .20000915; US 2000-231539P  20000911; US 2001-949650
     20010912
AB   WO 200220570 A UPAB: 20020701
     NOVELTY - Preventing (M1) interaction of human immunodeficiency virus
     (HIV)-1 viral protein R (Vpr) with adenine nucleotide
     translocator (ANT), comprising providing a molecule
     capable of preventing the binding of full-length Vpr to ANT, and
     contacting the molecule with an ANT fragment, where the molecule
     prevents the interaction of the ANT fragment with Vpr, is new.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
     following:
          (1) screening (M2) for molecules that compete with the binding of the
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C-terminal moiety of Vpr to **ANT**, comprising:

(a) providing a Vpr fragment capable of binding to **ANT**;

(b) contacting the Vpr fragment with an **ANT** fragment capable of binding to Vpr in the presence and absence of a test molecule; and

(c) detecting the binding of the Vpr fragment to the **ANT** fragment in the presence and absence of a test molecule;

(2) screening for molecules that mimic Vpr or Vpr fragments in its capacity to interact physically with **ANT**,comprising:

(a) providing a Vpr or Vpr fragment capable of interacting with **ANT**;

(b) contacting the Vpr or its fragment with an **ANT** fragment capable of interacting with Vpr or its fragment in the presence or absence of a test molecule; and

(c) detecting the binding of the Vpr or Vpr fragment to the **ANT** fragment in the presence or absence of a test molecule;

(3) a peptidic or non-peptidic molecule (I) that prevents or causes permeabilization of mitochondrial membranes, where the molecule prevents or enhances the binding of Vpr to **ANT**;

(4) a pharmaceutical and diagnostic composition (C) comprising (I);

(5) screening for genetic or epigenetic alterations in the expression or structure of the three **ANT** isoforms in humans, comprising:

(a) providing a fragment of Vpr, where the fragment is capable of binding to **ANT**, with a sample comprising human **ANT**;

(b) mixing the fragment with a biological and control samples comprising human **ANT**;

(c) detecting the binding of Vpr to **ANT** in the biological sample and the control sample;

(d) correlating a difference in binding with a genetic or epigenetic alteration of **ANT**; and

(e) optionally detecting a difference in the **ANT** capacity to form channel in liposome or in planar lipids bilayers;

(6) quantifying the level of the three human **ANT** isoforms in a cell, by mixing Vpr with a biological sample comprising **ANT** in an amount effective to bind to **ANT**, and quantitating the level of binding of Vpr to **ANT**;

(7) screening (M3) active molecules of interest that induce to prevent formation of a lethal pore by **ANT**, comprising:

(a) providing purified **ANT** in artificial lipid bilayers or liposomes;

(b) contacting molecules of interest to be screened with the **ANT**; and

(c) detecting lethal pore formation by measuring the release of labeled substrate;

(8) screening active molecules of interest that inhibit the formation of a lethal pore without preventing antiport function, comprising:

(a) providing a composition comprising purified **ANT** in artificial lipid bilayers or liposomes with a molecule that induces the formation of a lethal pore;

(b) contacting the composition in the presence or absence of a test molecule;

(c) detecting by fluorescence the presence of the antiport function; and

(d) detecting by another fluorescence the test molecule that inhibits the formation of a lethal pore; and

(9) an isolated or purified peptide having the sequence (S1).

(S1) is Asp-Arg-His-Lys-Gln-Phe-Trp-Arg-Tyr-Phe-Ala-Gly-Asn.

ACTIVITY - None given.

MECHANISM OF ACTION - Modulator of physical and functional interaction between Vpr and ANT; modulator of mitochondrial membrane

permeabilization (claimed).
No biological data is given.
USE - M1 is useful for preventing channel formation in mitochondrial membranes and permeabilization of mitochondrial membranes. M1 is also useful for preventing cell death by apoptosis. (C) is useful for causing or preventing permeabilization of mitochondrial membranes. (All claimed).
Dwg.0/9

TECH UPTX: 20020701
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The molecule in M1, is Bcl-2 or its fragment. The Vpr fragment comprises full length Vpr, or amino acids 52-96 of HIV-1 Vpr. The active molecule that induces the formation of a lethal pore is Vpr, its fragment or variant. Alternatively, the active molecule is **atractyloside**, mastoparan, terbutyl, diamide or pro-apoptotic molecules of Bcl-2 family e.g. a BAX molecule.

L7 ANSWER 2 OF 5 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-055598 [07] WPIDS
DNN N2002-040955 DNC C2002-015959
TI Novel recombinant expression construct for producing **adenine nucleotide translocator** polypeptides, comprises a regulated promoter linked to nucleic acid encoding the polypeptide.
DC B04 D16 S03
IN ANDERSON, C M; CARROLL, A K; CLEVENGER, W; DAVIS, R E; GHOSH, S S; MILLER, S W; MOOS, W H; PEI, Y; SZABO, T R; WILEY, S E
PA (MITO-N) MITOKOR
CYC 97
PI WO 2001085944 A2 20011115 (200207)* EN 147p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001061518 A 20011120 (200219)
EP 1283884 A2 20030219 (200321) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001085944 A2 WO 2001-US15416 20010511; AU 2001061518 A AU 2001-61518 20010511; EP 1283884 A2 EP 2001-935420 20010511, WO 2001-US15416 20010511
FDT AU 2001061518 A Based on WO 200185944; EP 1283884 A2 Based on WO 200185944
PRAI US 2000-569327 20000511
AB WO 200185944 A UPAB: 20020130
NOVELTY - A recombinant expression construct (I) comprising a regulated promoter operably linked to a nucleic acid encoding an **adenine nucleotide translocator** (**ANT**) polypeptide, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a host cell (II) comprising (I);
(2) an **ANT** polypeptide (III) produced by culturing a host cell infected with (I);
(3) an isolated **ANT** isoform polypeptide (IV);
(4) an isolated **ANT** isoform fusion protein (V) comprising (IV) fused to an additional polypeptide sequence;
(5) an isolated human or animal **ANT** fusion protein (VI) comprising **ANT** fused to an additional polypeptide sequence cleavable by a protease, where **ANT** is separable from the fusion protein by cleavage with the protease;
(6) determining the presence of (III) in a biological sample, by contacting sample suspected of containing (III) with an antibody and

detecting binding of the antibody;

(7) an **ANT** ligand (VII) comprising **atractyloside** substituted at the 6'hydroxyl to form an **atractyloside** derivative;

(8) an assay plate for high throughput screening of candidate agents that bind to an **ANT** polypeptide, comprising an assay plate having several wells, each of the wells further comprising at lest one immobilized recombinant **ANT** polypeptide, its variant or fragment;

(9) a pharmaceutical composition (IX) comprising (VII), (VIII) or an agent that binds to or interacts with **ANT** polypeptide identified by using the recombinant **ANT** polypeptide; and

(10) an **ANT** ligand (VIII) having the structure of formula (A) and stereoisomers and salts;

R1 = hydroxyl, halogen, OC(O)R4 or NHR4;

R2 = H or C(O)R5;

R3 = CH3 or =CH2;

R4 = -X-aryl, -X-substituted aryl, -X-arylalkyl, -X-substituted arylalkyl, X-heteroaryl, or -X-heteroarylalkyl;

X = optional amido or alkylamido linker moiety; and

R5 = alkyl.

ACTIVITY - None given.

MECHANISM OF ACTION - Binds and interacts with **ANT** polypeptide for mediating transport of ADP and ATP across the mitochondrial inner membrane. No supporting data is given.

USE - (I) is useful for producing recombinant **ANT** polypeptide by transforming a prokaryotic or eukaryotic host cell and culturing the host cell. (I) is also useful for targeting a polypeptide of interest to a mitochondrial membrane, where **ANT** polypeptide is expressed as a fusion protein with the polypeptide of interest. Recombinant **ANT** polypeptide or cell expressing the polypeptide is useful for identifying an agent that binds to an **ANT** polypeptide. **ANT** ligand is useful for determining the presence of an **ANT** polypeptide, preferably ANT1, ANT2 or ANT3 in a biological sample and for isolating **ANT** from a biological sample, where the **ANT** ligand is covalently or non-covalently bound to a solid phase. Detectably labeled **ANT** ligand is also useful for identifying an agent that interacts with an **ANT** polypeptide. Sample containing **ANT** is contacted with detectable **ANT** ligand in the presence of a candidate agent and binding of ligand to **ANT** in absence and presence of the agent is compared and an agent that interacts with **ANT** polypeptide is identified. (IX) is useful for treating a subject (all claimed).

Dwg.0/13

TECH UPTX: 20020130

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: **ANT** polypeptides are prepared by standard recombinant DNA technology. Preferred Construct: (I) is a recombinant viral expression construct and further comprises an additional nucleic acid sequence that regulates transcription and encodes a repressor of the regulated promoter. The **ANT** polypeptide comprises a **ANT** polypeptide from a mammal, such as rat, mouse, bovine or human, and is preferably ANT1, ANT2 or ANT3. The **ANT** polypeptide is expressed as a fusion protein with a product of a second nucleic acid sequence encoding a polypeptide cleavable by protease. The polypeptide product of the second nucleic acid sequence is an enzyme and the fusion protein localizes to mitochondrial membranes. Preferred Cell: (II) is a prokaryotic or eukaryotic cell such as yeast, insect, preferably Sf9 cell and Trichoplusia ni cell or a mammalian cell. The host cell lacks at least one isoform of an endogenous **ANT** and expression of the gene encoding an endogenous **ANT** isoform is substantially

impaired. Preferred Polypeptide: The **ANT** isoform polypetide is a recombinant ANT1 or ANT2, their variants or fragments. In (V) or (VI), the additional polypeptide sequence is a polypeptide having affinity for a ligand. Preferred Ligand: In (VII), the **atractyloside** is detectably substituted at 6' hydroxyl to form a detectable **atractyloside** derivative, preferably substituted with an amine or an amine containing functionality to form an amine modified **atractyloside** derivative. The detectable **atractyloside** derivative comprises a radiolabeled substituent such as 125I, 131I, 3H, 14C or 35S, or a fluorescent substituent or comprises covalently bound biotin. The **atractyloside** molecule is a **carboxyatractyloside** molecule that is substituted at 6'hydroxyl to form a **carboxyatractyloside** derivative. The **ANT** ligand further comprises a Eu3+ atom complexed to the **atractyloside** derivative.

L7 ANSWER 3 OF 5 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-291054 [30] WPIDS
DNC C2001-089349
TI New nucleic acid expression constructs, useful for screening for agents that alter mitochondrial permeability transition (MPT), comprises polynucleotide encoding MPT polypeptide or cyclophilin polypeptide fused to energy transfer molecule.
DC B04 D16
IN ANDREYEV, A Y; CLEVENGER, W; DAVIS, R E; FRIGERI, L G; MURPHY, A N; VELICELEBI, G; WILEY, S E; VELECELEBI, G
PA (MITO-N) MITOKOR
CYC 95
PI WO 2001032876 A2 20010510 (200130)* EN 154p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001013622 A 20010514 (200149)
EP 1228206 A2 20020807 (200259) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003516128 W 20030513 (200334) 216p
US 6562563 B1 20030513 (200335)
ADT WO 2001032876 A2 WO 2000-US30535 20001103; AU 2001013622 A AU 2001-13622 20001103; EP 1228206 A2 EP 2000-975595 20001103, WO 2000-US30535 20001103; JP 2003516128 W WO 2000-US30535 20001103, JP 2001-535558 20001103; US 6562563 B1 US 1999-434354 19991103
FDT AU 2001013622 A Based on WO 200132876; EP 1228206 A2 Based on WO 200132876; JP 2003516128 W Based on WO 200132876
PRAI US 1999-434354 19991103
AB WO 200132876 A UPAB: 20010603
NOVELTY - A nucleic acid expression construct (I) comprising a promoter operably linked to a polynucleotide encoding a mitochondrial permeability transition (MPT) pore component polypeptide fused to an energy transfer molecule (ETM) polypeptide or its variant, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid expression construct (II) comprising a promoter operably linked to a polynucleotide encoding a cyclophilin (Cyp) polypeptide fused to an ETM polypeptide or its variant;

(2) a polypeptide (III) comprising a MPT pore component polypeptide fused to an ETM polypeptide or its derivative;

(3) a polypeptide (IV) comprising a Cyp polypeptide fused to an ETM polypeptide or its derivative;

(4) a host cell (V) for identifying agents that alter MPT comprising (I) and (II), where binding of the MPT pore component to the Cyp polypeptide results in detectable energy transfer between the first and second ETM;

(5) screening (M1) for an agent that alters MPT comprising:

(a) contacting (V) containing a mitochondrian with a candidate agent and an inducer of MPT;

(b) exposing (V) to an excitation energy;

(c) detecting a level of energy transfer between the first and second ETM; and

(d) comparing the level of energy transfer to a first reference level generated in the absence of candidate agent and identifying an agent that alters MPT;

(6) detecting (M2) an agent that alters MPT comprising:

(a) contacting a CypD polypeptide with an **ANT** polypeptide and a candidate agent; and

(b) detecting a level of binding of CypD polypeptide to **ANT** polypeptide, relative to a level of binding detected in the absence of the candidate agent;

(7) an agent (VI) capable of altering MPT identified by M2;

(8) altering survival of a cell comprising contacting a cell with (VI);

(9) altering (M3) MPT comprising contacting a cell with (VI);

(10) preparing (III) or (IV) comprising culturing a host cell containing (I) or (II) respectively and recovering (III) or (IV) from the culture;

(11) a kit (VII) for screening for agents that alter MPT comprising:

(a) an isolated CypD polypeptide or its derivative;

(b) an isolated **ANT** polypeptide or its derivative; and

(c) a detection reagent that specifically binds to (a) or (b); and

(12) a kit (VIII) for screening for agents that alter MPT comprising a host cell, (I) and (II).

ACTIVITY - Neuroprotective; nootropic; antidiabetic; antiparkinsonian; ophthalmological; antipyschotic; cerebroprotective; cytostatic; antipsoriatic; auditory; anticonvulsant. No supporting data is given.

MECHANISM OF ACTION - Alter mitochondrial membrane permeability transition; alter interaction between mitochondrial **adenine nucleotide translocator** and cyclophilin D.

USE - The methods are useful for screening for agents that alter MPT and/or cell survival (claimed). These agents (VI) are useful for the prevention or treatment of diseases associated with altered mitochondrial function or dysfunctional cell survival, such as Alzheimer's disease, diabetes mellitus, Parkinson's disease, Huntington's disease, dystonia, Leber's hereditary optic neuropathy, schizophrenia, mitochondrial encephalopathy, lactic acidosis, stroke, cancer, psoriasis, hyperproliferative disorders, mitochondrial diabetes, deafness and myoclonic epilepsy ragged red fiber syndrome.

Dwg.0/14

TECH UPTX: 20010603

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Component: The MPT pore component is an **adenine nucleotide translocator** (**ANT**) (preferably human ANT1, human ANT2 or human ANT3), porin, hexokinase, creatine kinase, PRAX, CAML or the peripheral benzodiazepine receptor.

Preferred Polypeptide: The Cyp is CypD, human CypA, CypB, human CypC or human Cyp-60.

Preferred Molecule: The ETM is a (derivative of a) green fluorescent

protein (GFP) (e.g. blue-shifted GFP, cyan-shifted GFP, red-shifted GFP and yellow-shifted GFP), a FLASH sequence or an aequorin protein. Preferred Construct: (I) is a plasmid (e.g. pBAD-His, pEYFP-C1 and pECFP-N1), a cosmid, a shuttle vector, a viral vector or a vector containing a chromosomal origin of replication. The promoter is externally regulated.
Preferred Cell: (V) is a prokaryotic or eukaryotic cell, such as 293, COS-7, Sf9, Chinese Hamster Ovary (CHO), Hep-2, MDCK (undefined) or Jurkat. The first and second ETM have an excitation maximum of 300-650 nm and an emission maximum of 350-675 nm. The first and second ETM have excitation and emission maxima at different wavelengths. At least one nucleic acid construct is extrachromosomal or integrated into the host cell mitochondrial chromosome.
Preferred Method: M1 further comprises contacting (V) with an inhibitor of MPT (e.g. low pH, inducers of mitochondrial membrane potential and cyclosporin A) to generate a second reference level. Preferably (V) is contacted with **atractyloside** or bonkrekic acid or a compound that increases Ca+2 concentration in the mitochondria (e.g. ionophores, ionomycin, thapsigargin, amino acid transmitters, glutamate, N-methyl-D-aspartic acid, carbachol, apoptogens and inducers of potassium depolarization). (V) is further contacted with an inducer of oxidative stress (e.g. ethacrynic acid, buthionine, sulfoximine, diamide, menadione, t-butyl hydroperoxide, phenyl-arsine oxide and nitric oxide). The candidate agent increases or decreases energy transfer between the first and second ETM. The first ETM has an excitation maximum of 400-500 nm (preferably 433 nm) and an emission maximum of 450-525 nm (preferably 475 nm). The second ETM has an excitation maximum of 450-525 nm (preferably 513 nm) and an emission maximum of 500-550 nm (preferably 527 nm). Alternatively the second ETM has an excitation maximum of 400-450 nm (preferably 433 nm) and an emission maximum of 450-500 nm (preferably 475 nm). The first ETM has an excitation maximum of 500-525 nm (preferably 513 nm) and an emission maximum of 525-550 nm (preferably 527 nm). In M2 CypD and **ANT** polypeptide are immobilized on a support and are fusion proteins. They comprise a protease recognition sequence or a ligand for a receptor. The candidate agent is a (poly)peptide, protein or small molecule present within a combinatorial library. In M3 the mitochondrian is present within a cell or living organism. Preferably the cell is a cybrid cell.
Preferred Kit: In (VII) the CypD and **ANT** polypeptide are immobilized on a support. The detection reagent is an antibody or antigen-binding fragment.

L7 ANSWER 4 OF 5 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-071424 [08] WPIDS
DNN N2001-054040 DNC C2001-020049
TI Assaying mitochondrial membrane potential with energy transfer donor and acceptor molecules exogenous to the mitochondria, useful for identifying membrane potential modulating agents which are useful for treating diabetes and stroke.
DC B04 D16 S03
IN DYKENS, J A; GHOSH, S S; VELICELEBI, G
PA (MITO-N) MITOKOR
CYC 95
PI WO 2000079274 A2 20001228 (200108)* EN 189p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000057636 A 20010109 (200122)
US 6280981 B1 20010828 (200151)
US 6323039 B1 20011127 (200175)
EP 1210596 A2 20020605 (200238) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2003506014 W 20030218 (200315) 210p

ADT WO 2000079274 A2 WO 2000-US17380 20000622; AU 2000057636 A AU 2000-57636 20000622; US 6280981 B1 Div ex US 1999-338122 19990622, US 2000-514569 20000223; US 6323039 B1 US 1999-338122 19990622; EP 1210596 A2 EP 2000-943119 20000622, WO 2000-US17380 20000622; JP 2003506014 W WO 2000-US17380 20000622, JP 2001-505191 20000622

FDT AU 2000057636 A Based on WO 200079274; EP 1210596 A2 Based on WO 200079274; JP 2003506014 W Based on WO 200079274

PRAI US 2000-176383P 20000114; US 1999-140433P 19990622; US 1999-338122 19990622; US 2000-514569 20000223

AB WO 200079274 A UPAB: 20010207

NOVELTY - A new method (M1) for assaying mitochondrial membrane potential comprises contacting a mitochondrial sample with energy transfer donor and energy transfer acceptor molecules exogenous to the mitochondria, exciting the donor molecule and detecting a signal generated by energy transfer between the donor and acceptor molecules.

DETAILED DESCRIPTION - A new method (M1) for assaying mitochondrial membrane potential comprises contacting a mitochondrial sample with energy transfer donor and energy transfer acceptor molecules exogenous to the mitochondria, exciting the donor molecule and detecting a signal generated by energy transfer between the donor and acceptor molecules.

In detail, M1 comprises:

(a) contacting a sample comprising one or more mitochondria, simultaneously or sequentially and in either order, with each of a first and a second energy transfer molecule that is not endogenous to the mitochondria, where:

(i) the first and second energy transfer molecules each localize independently of one another to the same submitochondrial site or to acceptably adjacent submitochondrial sites, the sites being selected from the mitochondrial outer membrane, mitochondrial inner membrane, mitochondrial intermembrane space or mitochondrial matrix; and

(ii) the first energy transfer molecule is an energy donor molecule and the second energy transfer molecule is an energy acceptor molecule;

(b) exciting the energy donor molecule to produce an excited energy donor molecule; and

(c) detecting a signal generated by energy transfer from the first energy transfer molecule to the second energy transfer molecule, where the concentration of at least one of the energy transfer molecules in the mitochondria changes as a function of membrane potential.

INDEPENDENT CLAIMS are also included for the following:

(1) a method (M2) for identifying an agent that alters mitochondrial membrane potential, comprising:

(a) steps (a) to (c) of M1, where step (a) is carried out in the presence or absence of the test compound; and

(b) comparing the signal generated in the absence of the candidate agent to the signal generated in the presence of the candidate agent, and therefore identifying an agent that alters mitochondrial membrane potential;

(2) a method (M3) for identifying a regulator of an agent that alters mitochondrial membrane potential, comprising:

(a) steps (a) to (c) of M1, where step (a) is carried out in the presence or absence of the candidate regulator, and an agent that alters mitochondrial membrane potential or an agent identified by M2; and

(b) comparing the signal generated in the absence of the candidate

regulator to the signal generated in the presence of the candidate regulator, and therefore identifying a regulator that alters mitochondrial membrane potential;

(3) a method (M4) for identifying an agent that preferentially alters mitochondrial membrane potential in mitochondria from a first biological source without substantially altering mitochondrial membrane potential in mitochondria from a second biological source;

(4) a method (M5) of detecting the fusion of a first mitochondrion and a second mitochondrion;

(5) a method (M6) of identifying an agent that alters the fusion of mitochondria;

(6) a reagent for measuring mitochondrial Delta psi , comprising a FRET (fluorescence resonance energy transfer) donor molecule and a FRET acceptor molecule, where the accumulation of at least one of the molecules in mitochondria is dependent on Delta psi and the accumulation of the other molecules in mitochondria is independent of Delta psi ;

(7) a kit comprising the reagent of (6) and ancillary reagents for measuring mitochondrial Delta psi ;

(8) a method (M7) for assaying cellular membrane potential, comprising:

(a) steps (a) and (b) of M1, where the sample comprises at least one cellular membrane instead of the mitochondria and the first and second energy transfer molecules each localize independently of one another to the same membrane site or to acceptably adjacent membrane sites such that at least one of the energy transfer molecules localizes to a cellular membrane that forms a subcellular compartment; and

(b) detecting a signal generated by energy transfer from the first energy transfer molecule to the second energy transfer molecule, where the concentration of at least one of the energy transfer molecules in the membrane site changes as a function of membrane potential;

(9) a method (M8) for identifying an agent that alters a cellular membrane potential;

(10) a method (M9) for identifying a regulator of an agent that alters cellular membrane potential;

(11) a method (M10) for identifying an agent that preferentially alters a cellular membrane potential in a membrane from a first biological source (or sample) without substantially altering cellular membrane potential in a membrane from a second biological source (or sample);

(12) a method (M11) for detecting a specific type of cell in a sample, comprising:

(a) steps (a) and (b) of M1; and

(b) detecting a signal generated by energy transfer from the first energy transfer molecule to the second energy transfer molecule, where at least one of the energy transfer molecules preferentially accumulates in the specific type of cell and the signal correlates with the presence of the specific type of cell in the sample;

(13) a method (M12) for identifying a Delta psi m stabilizing agent;

(14) a Delta psi m stabilizing agent identified by M12; and

(15) a method (M13) of treating stroke comprising administering the Delta psi m stabilizing agent of (14) to a patient.

ACTIVITY - Nootropic; neuroprotective; antiparkinsonian; cytostatic; antipsoriatic; neuroleptic; cerebroprotective.

No biological data given.

MECHANISM OF ACTION - Mitochondrial membrane potential agonists and antagonists.

No biological data given.

USE - The method is used to develop assays of subcellular conditions or intracellular processes that are associated with diseases or disorders, e.g. Alzheimer's disease, Parkinson's disease or type II diabetes. The Delta psi m stabilizing agent is useful for treating stroke

(all claimed).

Agents that alters a mitochondrial or cellular membrane potential are useful for treating diabetes, Alzheimer's disease, Parkinson's disease, schizophrenia, stroke, hyperproliferative diseases such as cancer and psoriasis.

The methods are also useful for to identify and characterize such agents.

Dwg.0/24

TECH UPTX: 20010207

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The excited energy donor molecule transfers energy to the energy acceptor molecule to produce an excited energy acceptor molecule, and the signal detected in step (c) results from energy released by the excited energy acceptor molecule. The energy transfer from the first energy transfer molecule to the second energy transfer molecule results in a decrease in the detectable signal.

M1 further comprises contacting the mitochondria with an agent (i.e. an ionophore) that induces dissipation of mitochondrial membrane potential or an agent (e.g. CCCP (carbonyl cynaide m-chlorophenyl-hydrazone) and FCCP (carbonyl cyanide p-(trifluoromethoxy)phenyl-hydrazone)) that induces collapse of mitochondrial membrane potential. The sample is washed prior to the step of detecting a signal. The signal detected in step (c) is compared with a reference signal. The reference signal is generated by an indicator selected from an indicator of cell number, an indicator of mitochondrial mass, an indicator of cellular protein, an indicator of cellular DNA, an indicator of mitochondrial DNA, an indicator of mitochondrial protein or an indicator of fluid volume. The sample comprises one or more mitochondria that are present within at least one cell, and where the signal detected in step (c) is compared with a reference signal. The reference signal is generated from a subcellular site selected from a mitochondrial outer membrane, a mitochondrial inner membrane, a mitochondrial intermembrane space, a mitochondrial matrix, cytoplasm, nucleus, nuclear membrane or plasma membrane. Alternatively, the reference signal is generated from extracellular medium. The mitochondria are present within at least one cell during at least one step. The cell is an organism, a cultured cell, a cybrid cell, a plant cell or an animal cell.

The cell is present in a biological sample derived from a multicellular organism such as a plant or an animal such as a human. The human has, is suspected of having or is at risk of having a disease or disorder associated with organellar dysfunction, e.g. organellar dysfunction is mitochondrial dysfunction such as lysosomal dysfunction.

The first and second energy transfer molecules localize to a submitochondrial site selected from the mitochondrial matrix or mitochondrial inner membrane. The concentration of the first energy transfer molecule in the submitochondrial site does not change as a function of membrane potential, and the concentration of the second energy transfer molecule in the mitochondrial matrix decreases as a function of membrane potential.

The first energy transfer molecule (F1) has an excitation maximum at a wavelength of 373 nm to 390 nm, and an emission maximum at a wavelength of 400 nm to 500 nm and the second energy transfer molecule (S1) has an excitation maximum at a wavelength of 400 nm to 500 nm. F1 is a fusion protein comprising:

(a) a blue-shifted green fluorescent protein having a mutation in at least one of Phe-64, Ser-65, Tyr-66, Val-68 or Tyr-145; and

(b) a polypeptide sequence that localizes the fusion protein to a submitochondrial site.

S1 is selected from DASPEI (2-(4-(dimethylamino)styryl)-N-ethylpyridinium iodide), DASPMI (dimethylaminostyrylmethylpyridinium iodide), 4-Di-1-ASP (4-(4-(dimethylamino)styryl)-N-methylpyridinium iodide), 2-Di-1-ASP ASP

(2-(4-(dimethylamino)styryl)-N-methylpyridinium iodide), DiOC7(3) (3,3'-diheptyloxadicarbocyanine iodide), DiOC6(3) (3,3'-dihexyloxadicarbocyanine iodide), JC-1 (5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazoylcarbocyanine iodide) and SYTO (RTM) 18 yeast mitochondrial stain.

The first energy transfer molecule (F2) has an excitation maximum at a wavelength of 425 nm to 440 nm, and an emission maximum at a wavelength of 450 nm to 535 nm and the second energy transfer molecule (S2) has an excitation maximum at a wavelength of 450 nm to 530 nm. F2 is a fusion protein comprising:

(a) a cyan-shifted green fluorescent protein polypeptide having a mutation in at least one of Phe-64, Ser-65, Tyr-66, Asn-146, Met-153, Val-163 or Asn-212; and

(b) a polypeptide sequence that localizes the fusion protein to a submitochondrial site.

S2 is selected from DASPEI, 2-Di-1-ASP, DiOC6(3), SYTO (RTM) 18 yeast mitochondrial stain, rhodamine 6G, JC-1, NBD C6-ceramide or NBD C6-sphingomyelin

The first energy transfer molecule (F3) has an excitation maximum at a wavelength of 470 mn to 500 nm, and an emission maximum at a wavelength of 505 nm to 565 nm and the second energy transfer molecule (S3) has an excitation maximum at a wavelength of 505 nm to 565 nm. F3 is selected from nonylacridine orange (NAO), MitoTracker (RTM) Green FM, MitoFluor (RTM) Green, or a fusion protein, where the fusion protein comprises:

(a) a green fluorescent protein selected from a wildtype green fluorescent protein, a red-shifted green fluorescent protein having a mutation in one or more of Phe-64, Ser-65, Tyr-66, Gln-69, Ser-72 and Thr-203, or a yellow-shifted green fluorescent protein having a mutation in one or more of Phe-64, Ser-65, Tyr-66, Gln-69, Ser-72 or Thr-203; and

(b) polypeptide sequence that localizes the fusion protein to a submitochondrial site.

S3 is selected from rhodamine 123, JC-1, tetrabromorhodamine 123, rhodamine 6G, TMRM (tetramethylrhodamine, methyl ester), TMRE (tetramethylrhodamine, ethyl ester), tetramethylrosamine or rhodamine B.

The first energy transfer molecule (F4) has an excitation maximum at a wavelength of 545 mn to 560 nm, and an emission maximum at a wavelength of 565 nm to 625 nm and the second energy transfer molecule (S4) has an excitation maximum at a wavelength of 565 nm to 625 nm. F4 is selected from MitoTracker (RTM) Orange CMTMRos and S4 is DiOC2(5) (3,3'-diethyloxadicarbocyanine iodide).

The first energy transfer molecule (F5) has an excitation maximum at a wavelength of 495 mn to 510 nm, and an emission maximum at a wavelength of 510 nm to 570 nm and the second energy transfer molecule (S5) has an excitation maximum at a wavelength of 510 nm to 560 nm. F5 is selected from a fusion protein comprising:

(a) a polypeptide sequence selected from 'FLASH' (fluorescein arsenical helix binder) protein or a yellow-shifted green fluorescent protein sequence having a mutation in one or more of Ser-65, Tyr-66, Ser-72 or Thr-203; and

(b) a polypeptide sequence that localizes the fusion protein to a submitochondrial site.

S5 is selected from JC-1, tetrabromorhodamine 123, rhodamine 6G, TMRM, TMRE, tetramethylrosamine, rhodamine B or 4-dimethylamino-tetramethylrosamine.

A relative amount of the signal generated by energy transfer is detected. The signal is detected over a period of time and integrated, and a rate of change in the signal level is determined. The membrane potential comprises an electric potential, a pH potential, or both. The first and second energy transfer molecules localize to within 10 to 100, preferably 20 to 50, angstroms of each other. The signal is generated by fluorescence

resonance energy transfer.
In M3, the regulator is an agonist or antagonist of the agent that alters mitochondrial potential. The agent is an apoptogen, a thapsigargin, an ionophore (e.g. ionomycin or A23187), or an excitatory amino acid (e.g. glutamate, NAAG (undefined), NMDA (N-methyl-D-aspartate), AMPA (undefined), APPA (undefined) or kainate) or its derivatives.
M4 comprises:
(a) contacting, in the absence and presence of a candidate agent, a biological sample (from each biological source) comprising one or more mitochondria simultaneously or sequentially and in either order with a first and a second energy transfer molecule that is not endogenous to the mitochondria;
(b) steps (a)(i), (a)(ii), (b) and (c) of M1; and
(c) comparing the signal generated in each sample in the absence of the candidate agent to the signal generated in each sample in the presence of the candidate agent, and therefore identifying an agent that preferentially alters mitochondrial membrane potential.
The first and second biological samples are from distinct biological sources, preferably tissues. The first biological source is a mammal suspected of having, diagnosed as having or predisposed to having a disease, and the second biological source is a mammal that is not suspected of having and has not been diagnosed as having or predisposed to having the disease. The first and second biological sources are both human. The disease is Alzheimer's disease, Parkinson's disease or type II diabetes. When the biological source is a tissue, the first and second tissues are derived from the same subject, a subject of the same species or subjects of distinct species.
M5 comprises:
(a) contacting a first sample comprising one or more mitochondria with a first energy transfer molecule that is not endogenous to the mitochondria;
(b) contacting a second sample comprising one or more mitochondria with a second energy transfer molecule that is not endogenous to the mitochondria, where the first energy transfer molecule is an energy donor molecule and the second energy transfer molecule is an energy acceptor molecule;
(c) contacting the first sample with the second sample under conditions and for a time sufficient to permit mitochondrial fusion;
(d) exciting the energy donor molecule to produce an excited energy donor molecule; and
(e) detecting a signal generated by energy transfer from the first energy transfer molecule to the second energy transfer molecule, and therefore determining fusion of the first mitochondrion and the second mitochondrion;
M6 comprises:
(a) steps (a) and (b) of M5;
(b) carrying out step (c) of M5 in the presence and absence of the candidate agent;
(c) steps (d) of M5;
(d) detecting a signal generated by energy transfer from the first energy transfer molecule to the second energy transfer molecule; and
(e) comparing the signal detected in the absence of the candidate agent to the signal detected in the presence of the candidate agent, and therefore identifying an agent that alters the fusion of the mitochondria.
In M5 and M6, the first and second energy transfer molecules have the properties described in (a)(i) and (a)(ii) or M1.
In M2 to M5, the agent increases, dissipates or collapses mitochondrial membrane potential, or alters an equilibrium distribution of at least one ionic species (e.g. calcium) on either side of a cellular membrane (e.g. mitochondrial membrane). The agent (A1) that collapses mitochondrial membrane potential is an apoptogen and it interacts with an

adenine nucleotide translocator. A1 is an **atractyloside, carboxyatractyloside,** bongkrekic acid or isobongkrekic acid.

In M7, the first energy transfer molecule localizes to a first membrane site selected from mitochondria, endoplasmic reticulum, golgi, lysosome or plasma membrane and the second energy transfer molecule localizes to the same membrane site or to an acceptably adjacent membrane site selected from mitochondria, endoplasmic reticulum, golgi, lysosome or plasma membrane. The concentration of the first energy transfer molecule in the first membrane site does not change as a function of membrane potential, and the concentration of the second energy transfer molecule in the membrane site decreases as a function of membrane potential. The first energy transfer molecule is F1, F2, F3 or F4 and the second energy transfer molecule is S1, S2, S3 or S4, respectively.

M8 comprises:

(a) contacting, in the absence and presence of a candidate agent, a sample comprising one or more cellular membranes simultaneously or sequentially and in either order with each of a first and a second energy transfer molecule that is not endogenous to the sample, where:

(i) the first and second energy transfer molecules each localize independently of one another to the same membrane site or to acceptably adjacent membrane sites such that at least one of the energy transfer molecules localizes to a cellular membrane that forms a subcellular compartment, and

(ii) the first energy transfer molecule is an energy donor molecule and the second energy transfer molecule is an energy acceptor molecule;

(b) exciting the energy donor molecule to produce an excited energy donor molecule;

(c) detecting a signal generated by energy transfer from the first energy transfer molecule to the second energy transfer molecule, where the concentration of at least one of the energy transfer molecules in the subcellular compartment changes as a function of membrane potential; and

(d) comparing the signal generated in the absence of the candidate agent to the signal generated in the presence of the candidate agent, and therefore identifying an agent that alters cellular membrane potential.

M9 comprises:

(a) steps (a) to (c) of M8, where step (a) is carried out in the presence or absence of the candidate regulator, and an agent that alters cellular membrane potential or an agent identified by M8; and

(b) comparing the signal generated in the absence of the candidate regulator to the signal generated in the presence of the candidate regulator, and therefore identifying a regulator that alters mitochondrial membrane potential.

M10 comprises steps (a) and (b) of M4, where the biological sample (from each biological source) comprising one or more cellular membranes instead of one or more mitochondria. Step (c) comparing the signal generated in each sample in the absence of the candidate agent to the signal generated in each sample in the presence of the candidate agent, and therefore identifying an agent that preferentially alters cellular membrane potential. The first and second biological samples are from distinct biological sources, preferably tissues.

M11 further comprises comparing the signal generated in the sample with the signal generated from a control sample lacking the specific type of cell. The specific type of cell is a cancer cell

M12 comprises:

(a) contacting, in the absence and presence of a candidate DELTA(psi)m stabilizing agent, an agent that alters DELTA(psi)m and a sample comprising one or more mitochondria simultaneously or sequentially and in either order with each of a first and a second energy transfer molecule that is not endogenous to the mitochondria, where the energy transfer

molecules have the properties as described in (a)(i) and (a)(ii) of M1;
(b) steps (b) and (c) of M1;
(c) comparing the signal generated in the absence of the candidate DELTA(psi)m stabilizing agent, to the signal generated in the presence of the candidate DELTA(psi)m stabilizing agent, and therefore identifying DELTA(psi)m stabilizing agent.
The mitochondria are contained within cells. The agent that alters DELTA(psi)m is an agent that increases the level of cytosolic Ca2+. The agent that increases the level of cytosolic Ca2+ is selected from calcium ionophore or thapsigargin. The cells comprise one or more types of glutamate receptors. Alternatively, the agent that increases the level of cytosolic Ca2+ is an excitatory amino acid or its derivative, e.g. glutamate, NAAG, NMDA, AMPA, APPA and kainate.
In M1, M12 and M13, the cell is a permeabilized cell.
Preferred Reagent: The molecule that accumulates in mitochondria independent of DELTA(psi) is selected from NAO, MitoTracker (RTM) Green FM, MitoFluor (RTM), DAPI (4', 6-diamino-2-phenylindole), and a fusion protein comprising:
(a) a polypeptide selected from a red-shifted green fluorescent protein, a yellow-shifted green fluorescent protein and a 'FLASH' polypeptide, and
(b) a polypeptide sequence that localizes the fusion protein to the mitochondrial matrix or inner membrane.
The molecule that accumulates in mitochondria in a manner dependent on DELTA(psi) is selected of TMRM, TMRE, rhodamine 123, ethidum bromide, 4-Di-1-ASP, 2-Di-1-ASP or DASPEI.
The first FRET molecule that accumulates in mitochondria is formulated to dissolve to an extent necessary to saturate a population of cells in an aqueous solution with the first molecule within 0.01 to 2 minutes after being contacted with it, and the second molecule that accumulates in mitochondria is formulated to dissolve to an extent necessary to saturate a population of cells in an aqueous solution with the second molecule within 2.5 to 5 minutes after being contacted with it. One of the molecules that accumulates in mitochondria is dissolved in an aqueous solution, and the other of the molecules that accumulates in mitochondria is present in solid form in the reagent. The molecule that accumulates in mitochondria and that is present in solid form in the reagent is formulated to dissolve to an extent necessary to saturate a population of cells in an aqueous solution with the second molecule within 0.01 to 5 minutes after being contacted with it.

L7 ANSWER 5 OF 5 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-365619 [31] WPIDS
DNN N2000-273562 DNC C2000-110481
TI Recombinant construct encoding **adenine nucleotide translocator** polypeptide, useful e.g. in screening for potential therapeutic agents against mitochondrial disease.
DC B04 D16 S03
IN ANDERSON, C M; CLEVENGER, W; DAVIS, R E; GHOSH, S S; MILLER, S W; SZABO, T R; WILEY, S E; MOSS, W H; PEI, Y; MOOS, W H
PA (MITO-N) MITOKOR; (ANDE-I) ANDERSON C M; (CLEV-I) CLEVENGER W; (DAVI-I) DAVIS R E; (GHOS-I) GHOSH S S; (MILL-I) MILLER S W; (MOSS-I) MOSS W H; (PEIY-I) PEI Y; (SZAB-I) SZABO T R; (WILE-I) WILEY S E; (MOOS-I) MOOS W H
CYC 91
PI WO 2000026370 A2 20000511 (200031)* EN 174p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000024729 A 20000522 (200040)
EP 1049780 A1 20001108 (200062) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 2001044144 A1 20011122 (200176)
US 2002012992 A1 20020131 (200210)
AU 2002029293 A 20020523 (200245)#
AU 2002029295 A 20020523 (200245)#
AU 2002029271 A 20020523 (200246)#
AU 2002029273 A 20020523 (200246)#
AU 2002029276 A 20020516 (200247)#
AU 2002029290 A 20020516 (200247)#
US 2002177185 A1 20021128 (200281)
JP 2002539761 W 20021126 (200307) 192p

ADT WO 2000026370 A2 WO 1999-US25883 19991103; AU 2000024729 A AU 2000-24729 19991103; EP 1049780 A1 EP 1999-968032 19991103, WO 1999-US25883 19991103; US 2001044144 A1 CIP of US 1998-185904 19981103, Div ex US 1999-393441 19990908, US 2001-811094 20010314; US 2002012992 A1 CIP of US 1998-185904 19981103, Div ex US 1999-393441 19990908, US 2001-810644 20010314; AU 2002029293 A Div ex AU 2000-24729 19991103, AU 2002-29293 20020328; AU 2002029295 A Div ex AU 2000-24729 19991103, AU 2002-29295 20020328; AU 2002029271 A Div ex AU 2000-24729 19991103; AU 2002029273 A Div ex AU 2000-24729 19991103, AU 2002-29273 20020328; AU 2002029276 A Div ex AU 2000-24729 19991103, AU 2002-29276 20020328; AU 2002029290 A Div ex AU 2000-24729 19991103, AU 2002-29290 20020328; US 2002177185 A1 US 1998-185904 19981103; JP 2002539761 W WO 1999-US25883 19991103, JP 2000-579742 19991103

FDT AU 2000024729 A Based on WO 200026370; EP 1049780 A1 Based on WO 200026370; JP 2002539761 W Based on WO 200026370

PRAI US 1999-393441 19990908; US 1998-185904 19981103; US 2001-811094 20010314; US 2001-810644 20010314; AU 2002-29293 20020328; AU 2002-29295 20020328; AU 2002-29273 20020328; AU 2002-29276 20020328; AU 2002-29290 20020328

AB WO 200026370 A UPAB: 20020722

NOVELTY - Recombinant expression construct (A), comprising at least one regulated promoter (RP) linked to a nucleic acid (I) encoding an **adenine nucleotide translocator** (**ANT**) polypeptide (II), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a recombinant expression construct (A') containing at least one promoter (P) linked to (I) and to a second nucleic acid sequence (Ia), so that (II) is expressed as a fusion with the product of (Ia);

(2) a host cell containing (A) or (A');

(3) a method of production of recombinant (II), comprising culturing cells of (2);

(4) recombinant (II) produced by the method of (3);

(5) isolated human (II);

(6) a fusion protein (FP) of human or animal (II), with at least one additional polypeptide;

(7) a method for detecting (II) in a biological sample, comprising contacting a sample suspected of containing (II) with an **ANT** ligand, and detecting binding of the **ANT** ligand to (II), determining the presence of (III) in the sample;

(8) a method for isolating (II) from a biological sample by binding it to a ligand;

(9) a method for identifying an agent (III) that binds to (II), or host cells expressing it, comprising contacting a candidate agent with a host cell expressing (II), or a biological sample containing (II)and detecting binding of the agent to (II);

(10) a method for identifying an agent (IV) that interacts with (II), by incubating (II)-containing sample with detectable ligand and test compound, and comparing binding in absence and presence of test compound;

(11) a (II)-ligand comprising **atractyloside** derivatized by substitution at 6'-hydroxy;

(12) an **ANT** ligand having the structure:;

(13) an assay plate for high-throughput screening of test compounds for binding to (II) comprising many wells, each containing at least one immobilized recombinant (II), or its variants or fragments;

(14) targeting a polypeptide to mitochondrial membranes by expressing it as a fusion with (II); and

(15) a pharmaceutical composition comprising (II)-ligand of (11) or agents identified by the methods of (9) or (10).

R1 = hydroxy, hydrogen, -OCOR4;

R2 = hydrogen or -COR5;

R3 = methyl or =CH2;

R4 = -X-(aryl or arylalkyl (both optionally substituted), heteroaryl or heteroarylalkyl);

R5 = alkyl; and

X = optional amido or alkylamido linker moiety.

ACTIVITY - Neuroprotective; nootropic; antiParkinsonian; cytostatic; antidiabetic; anticonvulsant; antipsoriatic; cerebroprotective; neuroleptic.

MECHANISM OF ACTION - (II) mediate transport of adenosine di/tri-phosphates across the mitochondrial membrane and may also be part of the mitochondrial permeability transit pore, a modulator of apoptosis.

USE - (II) is used to identify agents or ligands that bind to, or interact with, it, and to target other polypeptides, in the form of fusion proteins, to the mitochondrial membrane (claimed). The identified ligands are used to detect or isolate (II), and therapeutically for the regulation of mitochondrial pore activity, potentially for treating diseases associated with altered mitochondrial function, including Alzheimer's, Parkinson's and Huntington's diseases, cancer, psoriasis, diabetes, dystonia, Leber's hereditary optic neuropathy, schizophrenia, michondrial encephalopathy, lactic acidosis, and stroke, hyperproliferative disorders, michondrial diabetes and deafness, and myoclonic epilepsy red ragged fiber syndrome.

ADVANTAGE - Recombinant production provides enough (II) to perform structural and functional assays.

Dwg.0/19

TECH UPTX: 20000630

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred constructs: (I) encodes a human (II), especially ANT1, 2 or 3, optionally as a fusion with, particularly, an enzyme. The fusion localizes to membranes, especially in mitochondria, and its second component may be released by proteolysis. In (A'), a nucleic acid sequence that regulates transcription may be included, particularly it encodes a repressor of the promoter. Preferred (A) are recombinant viral constructs.

Preferred method: The method of isolating (II) from a sample uses an **ANT** ligand covalently or non-covalently bound to a solid phase.

Preparation: Typically cDNA encoding (II) was amplified (primer sequences reproduced) and the product cloned into pBAD/His, containing the inducible, but tightly regulated araBAD promoter, optimized Escherichia coli transcription initiation sequence, polyHis and epitope tags and enterokinase cleavage site. The recombinant plasmid is then expressed in E. coli and the resulting fusion protein is localized in the bacterial membrane. More generally, any suitable vector/host system may be used.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred ligands: Ligands of (11) are particularly detectable, i.e. they carry a radioisotope such as 125I,

131I, 3H, 14C or 35S, a fluorescent label or covalently bound biotin. The ligand may have an Eu3+ atom complexed to the **atractyloside** derivative, for the fluorescent detection. Other derivatives are amino- or carboxy-modifications at 6' position. In the process (9), the ligand is (non-)covalently bound to a solid phase.
Preparation: The ligands are prepared from **atractyloside** by standard methods, e.g. acylation or (to introduce methyl) catalytic hydrogenation of =CH2.

L14 ANSWER 1 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-759941 [82] WPIDS
DNN N2002-598350 DNC C2002-214849
TI In vitro diagnosis and prognosis of inflammatory bowel disease, by determining expression of peroxysome proliferator-activated receptor gamma in the intestine.
DC **B04 D16 S03**
IN COLOMBEL, J F; DESREUMAUX, P; DUBUQUOY, L; COLOMBEL, J
PA (UYLI-N) UNIV LILLE CENT HOSPITALIER REGIONAL
CYC 100
PI WO 2002077651 A1 20021003 (200282)* FR 35p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
FR 2822955 A1 20021004 (200282)
ADT WO 2002077651 A1 WO 2002-FR1076 20020327; FR 2822955 A1 FR 2001-4128 20010327
PRAI FR 2001-4128 20010327
AB WO 200277651 A UPAB: 20021220
NOVELTY - In vitro determination of the amount of expression product (I) from the peroxysome proliferator-activated receptor gamma (PPARc) gene (II) in a sample of intestinal tissue that contains at least cells from the epithelium and/or lamina propria (LP).

DETAILED DESCRIPTION - In vitro determination of the amount of expression product (I) from the peroxysome proliferator-activated receptor gamma (PPARc) gene (II) in a sample of intestinal tissue that contains at least cells from the epithelium and/or lamina propria (LP). The sample, from a subject with, or developing, an inflammatory bowel disease, is treated with a compound (III), **labeled** or capable of being **labeled**, that binds specifically to (I) to form a complex, then the signal from the **label** is quantified and, for localization, visualized.

INDEPENDENT CLAIMS are also included for the following:

(1) diagnostic composition containing a mono- or poly-clonal antibody (Ab) or a natural or synthetic (**ant**)agonistic **ligand** directed against PPARc, or a nucleic acid that hybridizes specifically with a fragment of mRNA encoded by (II), all optionally **labeled**; and

(2) diagnostic kit containing the diagnostic composition and optionally appropriate reagents and/or a control sample.

USE - The method is used for diagnosis and prognosis of inflammatory bowel diseases, either chronic or acute, particularly Crohn's disease or, especially, hemorrhagic rectocolitis (HRC). It is based on the observation that expression of (II) is reduced in colonic mucosa in patients with HRC.

ADVANTAGE - The method is very sensitive and specific, almost 100% for diagnosis of HRC by immunohistochemical analysis, comparable with that for quantitative polymerase chain reaction or Western blotting, but much simpler and less expensive, so suitable for routine use.
Dwg.0/2

TECH UPTX: 20021220
TECHNOLOGY FOCUS - BIOLOGY - Preferred Process: The sample contains cells from both epithelium and LP, and the distribution of (I) between these cell types is determined. It may be taken from the colon (most preferred) or small intestine. To determine (I) that is a protein, either:
(i) total proteins are extracted from the sample, separated (by electrophoresis), transferred to a membrane and tested for reaction with a specific antibody (or ligand); or
(ii) especially preferred for diagnosis of hemorrhagic rectocolitis (HRC), a section of the sample, optionally fixed, is stained and the signal observed.
The size of the signal, optionally also its distribution, is compared with that in a control sample, especially from a healthy subject or from a patient known to have a chronic inflammatory bowel disease. A reduction in expression of (I) is indicative of inflammatory disease.
Preferred Materials: (I) may be a protein and (III) is then a specific antibody or ligand (e.g. prostaglandin J2 or polyunsaturated fatty acid). Alternatively it is mRNA and (III) is then a specifically hybridizing nucleic acid.

L14 ANSWER 2 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-616690 [71] WPIDS
DNN N2001-459963 DNC C2001-184716
TI Biosensor chip, useful for detecting e.g. protein or nucleic acid, has two electrodes for performing reduction-oxidation recycling process and integrated differentiation circuit.
DC **B04 D16 S03**
IN FREY, A; THEWES, R
PA (INFN) INFINEON TECHNOLOGIES AG
CYC 22
PI WO 2001075141 A2 20011011 (200171)* DE 65p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: JP US
DE 10015816 A1 20011018 (200171)
EP 1272850 A2 20030108 (200311) DE
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
ADT WO 2001075141 A2 WO 2001-DE1241 20010329; DE 10015816 A1 DE 2000-10015816 20000330; EP 1272850 A2 EP 2001-927637 20010329, WO 2001-DE1241 20010329
FDT EP 1272850 A2 Based on WO 200175141
PRAI DE 2000-10015816 20000330
AB WO 200175141 A UPAB: 20011203
NOVELTY - Biosensor chip (A) with an electrode (E1), comprising a region for retaining probes (I) able to bind to macromolecular biopolymers (II) and an electrode (E2), configured so that a reduction/oxidation recycling process can occur on them, is new. The chip has an integrated electrical differentiator circuit that detects the current generated during the process and differentiates it with respect to time.
USE - The chip is used to detect proteins, peptides and nucleic acids.
ADVANTAGE - (A) provides reliable determination of the slope of the current/time plot generated during the redox process. On-chip differentiation is a more robust system than the conventional off-chip differentiation and the chip can provide quantitative information.
Dwg.0/19

TECH UPTX: 20011203

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Chip: This includes a third electrode (E3) and electrodes are at potential which ensure that the process occurs only on E2 and E3, especially E3 has the highest potential and E2 the lowest. The (I)-retaining region of E1 is coated with a material able to immobilize (I), particularly gold, silver, or it carries hydroxy, epoxy, and amino. as functional groups. The electrodes may have an interdigitated arrangement with E3 positioned between E1 and E2, and the arrangement ensures that the field lines between the electrodes are essentially straight. The differentiation circuit is connected to E2, preferably through a current-voltage converter, and (A) also includes a reference circuit (similar to the differentiation circuit) to provide an electrical reference signal. The chip also includes a unit that evaluates signals from these two circuits to determine the gradient of the plot of current against time. Optionally, many electrodes can be combined, forming an array.
Preferred Process: The chip is first treated with test solution, then rinsed and treated with a solution containing a substrate that is cleaved by an enzyme **label** of (II). The substrate is cleaved to two fragments, having different electrical charges, and these undergo reduction or oxidation on the electrodes.
Preferred Materials: Where (II) is a protein or peptide, (I) is an appropriate **ligand**, e.g. enzyme (**ant**)agonist, pharmaceutical, sugar or antibody, and when (II) is DNA, (I) is a probe. Typical enzymes are galactosidase and phosphatase and substrates, correspondingly, p-aminophenyl-hexopyranosides or -phosphates.

L14 ANSWER 3 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-328869 [34] WPIDS
CR 2001-343541 [36]
DNN N2001-236663 DNC C2001-100935
TI New transgenic animals, useful to screen for weight regulators for treatment of various disorders including obesity, comprises non-functional melanocortin-3 receptor protein and increased body fat.
DC **B04 D16** P14
IN CHEN, A S; CHEN, H Y; VAN DER PLOEG, L H; VAN DER PLOEG, L H T
PA (MERI) MERCK & CO INC
CYC 94
PI WO 2001033954 A1 20010517 (200134)* EN 50p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001017584 A 20010606 (200152)
EP 1241933 A1 20020925 (200271) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2003513645 W 20030415 (200328) 112p
ADT WO 2001033954 A1 WO 2000-US30746 20001109; AU 2001017584 A AU 2001-17584 20001109; EP 1241933 A1 EP 2000-980304 20001109, WO 2000-US30746 20001109; JP 2003513645 W WO 2000-US30746 20001109, JP 2001-535975 20001109
FDT AU 2001017584 A Based on WO 200133954; EP 1241933 A1 Based on WO 200133954; JP 2003513645 W Based on WO 200133954
PRAI US 2000-220713P 20000726; US 1999-165074P 19991112; US 1999-165141P 19991112
AB WO 200133954 A UPAB: 20030501
NOVELTY - A transgenic non human animal (T1), whose somatic and germ cells are homozygous for an altered melanocortin-3 receptor (MC-3R) gene which encodes a non-functional MC-3R protein, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a cell line derived from T1;

(2) a transgenic mouse whose somatic cells are hemizygous for an altered MC-3R gene;

(3) a cell line derived from the above mouse;

(4) a viable transgenic mouse whose somatic and germ cells lack a functional gene encoding a murine MC-3R protein and which contain and express a transgene comprising a gene for a non-native MC-3R protein;

(5) producing a mouse having somatic and germ cells that lack a murine gene encoding MC-3R, comprising:

(a) providing a gene encoding an altered form of MC-3R designed to target a MC-3R allele of mouse embryonic stem cells;

(b) introducing the altered gene into mouse embryonic stem cells;

(c) selecting cells containing the altered gene and introducing them to mouse blastocysts;

(d) transplanting the blastocysts into a pseudopregnant mouse; and

(e) allowing the embryo to develop to term to produce a chimeric founder transgenic mouse;

(6) a transgenic non human animal whose somatic and germ cells are homozygous for an altered MC-3R gene encoding a non-functional MC-3R protein and homozygous for an altered MC-4R gene encoding a non-functional MC-4R protein;

(7) a cell line derived from the above transgenic animal;

(8) a transgenic mouse whose somatic cells are homozygous or heterozygous for an altered MC-3R gene and an altered MC-4R gene both expressing a non-functional protein;

(9) a cell line derived from the above transgenic animal;

(10) a viable transgenic mouse whose somatic and germ cells lack a functional gene encoding a murine MC-3R and MC-4R protein and which contain and express transgenes comprising a gene for a non-native MC-3R protein and a non-native MC-4R protein;

(11) determining if a substance can bind to MC-3R, comprising:

(a) transfecting cells with an expression vector for MC-3R expression;

(b) exposing the cells to a test substance; and

(c) measuring binding of the substance to MC-3R where a substance which binds is identified as one which potentially regulates body weight;

(12) determining if a substance can activate MC-3R and regulate body weight, comprising:

(a) transfecting cells with an expression vector for MC-R3 expression;

(b) exposing the cells to a test substance; and

(c) measuring accumulated intracellular cyclic adenosine monophosphate (cAMP);

(13) identifying a substance which modulates MC-3R receptor activity and body weight, comprising combining the substance in the presence and absence of a MC-3R protein having the 360 amino acid sequence fully defined in the specification, and comparing the effects;

(14) determining if a substance is a potential (ant)agonist of MC-3R and regulates body weight, comprising:

(a) transfecting/transforming cells with an MC-3R expression vector so that MC-3R is expressed;

(b) exposing the cells to **labeled** ligand of M3R in the presence and absence of the substance; and

(c) measuring binding of the ligand;

(15) determining if a substance is capable of binding to MC-3R and regulates body weight, comprising, transfecting/transforming cells with an MC-3R expression vector, exposing the cells to the substance, and detecting binding;

(16) determining if a substance is capable of binding to MC-3R and regulating body weight, comprising:
(a) transfecting/transforming cells with an MC-3R expression vector;
(b) preparing membranes containing MC-3R from the cells;
(c) exposing the membranes to a ligand of MC-3R so that binding takes place;
(d) exposing the membranes to the test substance; and
(e) measuring ligand binding in the presence/absence of the substance;
(17) determining if a substance is capable of binding to MC-3R and regulating body weight, comprising
(a) transfecting/transforming cells with an MC-3R expression vector;
(b) preparing membranes containing MC-3R from the cells;
(c) measuring binding of the substance to the MC-3R in the membranes; and
(d) comparing binding to binding of substance to membranes from control cells;
(18) identifying potential (ant)agonists of MC-3R which regulate body weight, comprising:
(a) transfecting/transforming cells with an MC-3R expression vector and a second expression vector for a promiscuous G-protein, or a vector encoding a chimeric MC-3R protein fused at its C terminus to a promiscuous G-protein;
(b) exposing cells to a test substance; and
(c) measuring the level of inositol phosphates in the cells where a decrease indicates an antagonist and an increase indicates an agonist; and
(19) selecting a compound which shows in vivo efficacy for modulation of MC-3R and regulation of body weight, comprising administering a compound selected by one of the above methods to a non-human animal and measuring the effect on body weight.
USE - The invention provides knock-out mice to screen for MC-3R modulators useful to treat obesity, diabetes mellitus, hypertension, hyperlipidemia, osteoarthritis, cancer, gall bladder disease, sleep apnea, depression, anxiety, compulsion, neuroses, insomnia/sleep disorder, substance abuse, pain, sexual dysfunction, fever, inflammation, immunomodulation, rheumatoid arthritis, learning memory, modulation of cytokine release, skin tanning, acne and other skin disorders, neuroregeneration and neuroprotective and cognitive memory enhancement including the treatment of Alzheimer's disease.
Dwg.0/29

TECH UPTX: 20010620
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Mouse: The homozygous transgenic mice are preferably fertile and capable of transferring the altered gene(s) on to their offspring. Preferably the mice exhibit a disorder which is either diabetes, male or female sexual dysfunction, pain, memory, neural regeneration and neuropathy, growth disorders related to growth hormone (GH), IGF1 (undefined) function or other states resulting from GH deficiency, or most preferably an obesity syndrome.

L14 ANSWER 4 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-273578 [28] WPIDS
DNN N2001-195393 DNC C2001-082998
TI New primate, particularly human vomeronasal-like receptor, homologous to rat and mouse pheromone receptors, useful to screen for (ant)agonists and to identify receptor subtype selective ligands.
DC **B04 D16 S03**
IN MOMBAERTS, P; RODRIGUEZ, I
PA (UYRQ) UNIV ROCKEFELLER
CYC 93
PI WO 2001025431 A1 20010412 (200128)* EN 82p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000077489 A 20010510 (200143)

ADT WO 2001025431 A1 WO 2000-US27211 20000929; AU 2000077489 A AU 2000-77489 20000929

FDT AU 2000077489 A Based on WO 200125431

PRAI US 2000-640209 20000816; US 1999-157267P 19991001; US 2000-225543 20000816

AB WO 200125431 A UPAB: 20011129

NOVELTY - An isolated primate vomeronasal-like receptor, particularly a human vomeronasal-like receptor (hVLR1), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an antigenic fragment of hVLR1;

(2) a chimeric polypeptide (I) comprising an amino acid sequence of hVLR1 fused to a heterologous amino acid sequence;

(3) a nucleic acid (II) encoding VLR1 or (I);

(4) an isolated nucleic acid (III) comprising a nucleotide sequence corresponding to or complementary to at least 10 base length of (II);

(5) a vector (IV) comprising (II);

(6) a host cell comprising (IV);

(7) producing hVLR1;

(8) an isolated host cell that expresses hVLR1, which is not a human cell that endogenously express the receptor;

(9) a non-human animal that expresses hVLR1;

(10) an antibody that specifically binds to hVLR1;

(11) identifying (V) a compound that binds to hVLR1, comprising detecting association of a candidate compound with the receptor, where detection of the association indicates that the compound binds to the receptor;

(12) detecting a compound that agonizes hVLR1, comprising detecting G-protein activation in a cell that expresses the receptor when the cell is contacted with a compound that binds to the receptor;

(13) detecting expression of hVLR1 in a cell comprising detecting the presence of mRNA encoding the receptor or the receptor in the cell; and

(14) identifying (VI) an allelic variant of a gene encoding hVLR1, comprising detecting a polymorphism in a gene encoding hVLR1, when compared to sequence of a gene encoding hVLR1.

USE - hVLR1 peptide sequences are useful for generating antibodies which are useful for activating the receptor by aggregating them and in assays for identifying ligands. Nucleic acid encoding hVLR1 is useful for developing high throughput screens to identify new pheromone-like (**ant**)agonists, receptor subtype selective **ligands** and to make chimeric and mutant vomeronasal-like receptors which can be useful to identify critical ligand binding domains as well as to determine selectivity of ligands. The DNAs are further useful for investigating signal transduction systems of vomeronasal-like receptors as well as to determine tissue distribution of receptors. Cells or whole animals expressing the gene encoding hVLR1 are useful in screening methods to identify candidate drugs, particularly (ant)agonists selective for VLR1.

Dwg.0/7

TECH UPTX: 20010522

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preparation: hVLR1 is prepared by culturing the host cell comprising (IV) under conditions that permit expression of the receptor (claimed).

Preferred Polypeptide: In (I) the heterologous amino acid sequence has

functional activity of a signal peptide, antibody tag, expression tag, chromatographic tag, cytoplasmic signal domain or G-protein binding domain.
Preferred Nucleic Acid: (II) hybridizes under high stringent conditions to a nucleic acid having a sequence corresponding to or complementary to a nucleic acid sequence of 942 or 1059 base pairs (bp) fully defined in the specification. (III) is single stranded, **labeled** and hybridizes under intracellular conditions to an mRNA encoding hVLR1. (III) has a sequence chosen from:
(1) CTIAGYCCIAGRAGYTCITG;
(2) ATMGCIACICCIAAYTRAC;
(3) AARGCITCICCIGARCARAGRGCIAC;
(4) ARIARIGCIACCATRTAIC;
(5) CKIGTIGCYCTYTGYTCIGG;
(6) ACRAAIGGRCTIACIGTIGCRTA;
(7) TCRGGIAARCAITADWSITG;
(8) ARIATIGTYCTIGTIGCYCTYTG;
(9) TTCTCTGCAGTTGGACACACAAGC and
(10) GCAAGAGTTATGATAAATAGCTG.
Preferred Vector: The nucleic acid encoding hVLR1 is operatively associated with an expression control sequence that permits expression of the receptor in a host cell.
Preferred Method: In (V), the receptor is present in a membrane of the cell. The compound is **labeled** and modulates receptor signaling when bound to the receptor. (VI) involves detecting a polymorphism in the gene encoding hVLR1 by sequencing.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: hVLR1 polypeptides can be prepared by standard chemical methods including solid phase synthesis or peptide condensation techniques.

L14 ANSWER 5 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-423511 [36] WPIDS
DNN N2000-315968 DNC C2000-128313
TI Identifying HDPXU17 receptor agonists or antagonists for treating cancer, neurological disorders, etc. comprises determining activatory or inhibitory activity of a test compound on the cell surface expressed polypeptide.
DC **B04 D16 S03**
IN BERGSMA, D J; CULP, J S; HALSEY, W S; SATHE, G; WANG, D
PA (SMIK) SMITHKLINE BEECHAM CORP
CYC 20
PI WO 2000034783 A1 20000615 (200036)* EN 46p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP
EP 1137938 A1 20011004 (200158) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000034783 A1 WO 1999-US28941 19991207; EP 1137938 A1 EP 1999-964135 19991207, WO 1999-US28941 19991207
FDT EP 1137938 A1 Based on WO 200034783
PRAI US 1998-297493 19981208
AB WO 200034783 A UPAB: 20000801
NOVELTY - Agonist or antagonist of HDPXU17 receptor polypeptide (I) identified by contacting a test compound with cells expressing (I) on the surface associated with a signal generating component and determining the activation or inhibition of (I) by measuring the level of signal generated from interaction of the compound with (I).
DETAILED DESCRIPTION - (I) or a polypeptide with 95% identity to (I) has a fully defined 374 amino acid sequence (given in the specification).
An INDEPENDENT CLAIM is also included for identifying an (ant)agonist

of (I) comprising:

(a) determining the inhibition of binding of a ligand to cells or cell membranes that express or contain (I), in the presence of a test compound under conditions to permit binding to the polypeptide; and

(b) determining the amount of ligand bound to (I), such that the compound capable of causing reduction of binding of a **ligand** is an (**ant**)agonist.

ACTIVITY - Antiasthmatic; antidiabetic; antimicrobial; cytostatic; neuroprotective; osteopathic; cardiant; anorectic.

MECHANISM OF ACTION - Regulator of HDPXU17 activity.

USE - The method is useful for identifying an (ant)agonist of a HDPXU17 polypeptide. The (ant)agonist is useful for treating abnormal conditions associated with excess of insufficient amounts of HDPXU17 activity such as bacterial, fungal or viral infections, cancer, diabetes, Parkinson's disease, asthma, myocardial infarction, osteoporosis, leukemia and neurological disorders.

Dwg.0/0

TECH UPTX: 20000801

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: The method further comprises conducting the identification in the presence of **labeled** or unlabeled dATP, dAMP or UTP.

L14 ANSWER 6 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1999-337714 [28] WPIDS
DNN N1999-253082 DNC C1999-099318
TI Secreted protein NSL4 for encoding DNA and treating various illnesses.
DC **B04 D16 S03**
IN GALLAGHER, K T; KIKLY, K K; MCLAUGHLIN, M M; SOUSA, S; STOCKWELL, S
PA (SMIK) SMITHKLINE BECKMAN CORP; (SMIK) SMITHKLINE BEECHAM CORP
CYC 21
PI WO 9924601 A1 19990520 (199928)* EN 44p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US
EP 1038020 A1 20000927 (200048) EN
R: BE CH DE DK FR GB IT LI NL
JP 2001521761 W 20011113 (200204) 45p
ADT WO 9924601 A1 WO 1998-US24243 19981112; EP 1038020 A1 EP 1998-957922 19981112, WO 1998-US24243 19981112; JP 2001521761 W WO 1998-US24243 19981112, JP 2000-519594 19981112
FDT EP 1038020 A1 Based on WO 9924601; JP 2001521761 W Based on WO 9924601
PRAI US 1997-65139P 19971112
AB WO 9924601 A UPAB: 20000516

NOVELTY - Secreted protein NSL4 (A) comprising the 192 residue amino acid sequence given in the specification, is new.

DETAILED DESCRIPTION - An isolated polypeptide (A) selected from:

(a) an isolated polypeptide comprising an amino acid sequence selected from peptides having at least:

(i) 70% identity;

(ii) 80% identity;

(iii) 90% identity; or

(iv) 95% identity to the 192 residue amino acid sequence given in the specification;

(b) an isolated polypeptide comprising the 192 residue amino acid sequence; or

(c) an isolated polypeptide which is the 192 residue amino acid sequence.

INDEPENDENT CLAIMS are also included for:

(1) an isolated polynucleotide selected from:

(i) an isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide that has at least:

(a) 70% identity;
(b) 80% identity;
(c) 90% identity; or
(d) 95% identity to the 192 residue amino acid sequence given in the specification;
(ii) an isolated polynucleotide comprising a nucleotide sequence that has at least:
(a) 70% identity;
(b) 80% identity;
(c) 90% identity; or
(d) 95% identity to a nucleotide sequence encoding the 192 residue amino acid sequence given in the specification;
(iii) an isolated polynucleotide comprising a nucleotide sequence which has at least:
(a) 70% identity;
(b) 80% identity;
(c) 90% identity; or
(d) 95% identity to the 1039 bp DNA sequence given in the specification;
(iv) an isolated polynucleotide comprising a nucleotide sequence encoding the 192 residue amino acid sequence;
(v) an isolated polynucleotide which is the 1039 bp DNA sequence; or
(vi) an isolated polynucleotide obtainable by screening an appropriate library under stringent hybridisation conditions with a **labeled** probe having the 1039 bp sequence or a fragment of it; or
(vii) a nucleotide sequence complementary to the isolated polynucleotide.
(2) an antibody immunospecific for (A);
(3) a method for the treatment of a subject:
(a) in need of enhanced activity or expression of (A), comprising:
(i) administering to the subject a therapeutically effective amount of an agonist to (A), and/or
(ii) providing to the subject an isolated polynucleotide comprising a nucleotide sequence encoding the polypeptide in a form so as to effect production of the polypeptide activity in vivo; or
(b) having need to inhibit activity or expression of (A), comprising:
(i) administering to the subject a therapeutically effective amount of an antagonist of (A);and/or
(ii) administering to the subject a nucleic acid molecule that inhibits the expression of a nucleotide sequence encoding the polypeptide,and/or
(iii) administering to the subject a therapeutically effective amount of a polypeptide that competes with (A) for its ligand, substrate, or receptor;
(4) a process for diagnosing a disease or a susceptibility to a disease in a subject related to expression or activity of (A) in a subject, comprising:
(a) determining the presence or absence of a mutation in the nucleotide sequence encoding the polypeptide in the genome of the subject; and/or
(b) analyzing for the presence of amount of the polypeptide expression in a sample derived from the subject;
(5) a method for screening to identify compounds which stimulate of which inhibit the function of (A), comprising a method selected from:
(a) measuring the binding of a candidate compound to the polypeptide (or to the cells or membranes beating the polypeptide) or a fusion protein, by means of a label directly or indirectly associated with the candidate compound;
(b) measuring the binding of a candidate compound in the presence of a labeled competitor;

(c) testing whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells or cell membranes bearing the polypeptide;

(d) mixing a candidate compound with a solution containing (A) to form a mixture, measuring the activity of the polypeptide in the mixture and comparing the activity of the mixture to a standard; or

(e) detecting the effect of a candidate compound on the production of mRNA encoding the polypeptide and the polypeptide in cells, using for instance, an ELISA assay;

(6) an agonist or an antagonist of (A);

(7) an expression system comprising a polynucleotide capable of producing (A) when the expression system is present in a compatible host cell;

(8) a process for producing a recombinant host cell, comprising transforming or transfecting a cell with the expression system of (7) so that the host cell under appropriate conditions produces (A);

(9) a recombinant host cell produced by the process of (8)

(10) a membrane of the recombinant host cell of (9), expressing (A);

(11) an isolated polynucleotide selected from:

(a) an isolated polynucleotide comprising a nucleotide sequence which has at least 70%, 80%, 90%, 95%, 97% identity to the 172 bp DNA sequence given in the specification;

(b) an isolated polynucleotide comprising the 172 bp sequence; or

(c) an isolated polynucleotide comprising a nucleotide sequence encoding a polypeptide which has at least 70%, 80%, 90%, 95%, 97-99% identity to the 38 residue amino acid sequence given in the specification; and

(12) a polypeptide selected from:

(a) a polypeptide which comprises an amino acid sequence which has at least 70%, 80%, 90%, 95%, 97-99% identity to the 38 residue sequence;

(b) the 38 residue sequence; or

(c) a polypeptide which is encoded by a polynucleotide comprising the 172 bp DNA sequence.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The host cell of (9) can be used to produce (A) (claimed). (A), the DNA encoding it, and (ant)agonists of it can be used for treating bacterial, fungal, protozoan and viral infections; pain; cancers; anorexia; bulimia; asthma; Parkinson's disease; acute heart failure; hypertension; hypertension; urinary retention; osteoporosis; angina pectoris; myocardial infarction; ulcers; asthma; allergies; benign prostatic hypertrophy; and psychotic and neurological disorders, including anxiety, schizophrenia, manic depression, delirium, severe mental retardation and dyskinesias, such as Huntington's disease or Gilles dela Tourett's syndrome.

ADVANTAGE - None given.

Dwg.0/0

L14 ANSWER 7 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1999-276975 [23] WPIDS
DNC C1999-081267
TI Polypeptide 8F4 co-stimulates T cells and is present only on activated cells.
DC A14 A96 **B04 D16**
IN KROCZEK, R
PA (BUND) BUNDESREPUBLIK DEUT; (DEKO-N) DEUT KOCH INST ROBERT; (BUND) BUNDESREPUBLIK DEUT PAUL-EHRLICH-INST
CYC 84
PI WO 9915553 A2 19990401 (199923)* DE 46p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

DE 19821060 A1 19990415 (199923)
AU 9913320 A 19990412 (199934)
EP 1017723 A2 20000712 (200036) DE
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2001517425 W 20011009 (200174) 51p
AU 752433 B 20020919 (200272)
US 2002177191 A1 20021128 (200281)
US 2002182667 A1 20021205 (200301)

ADT WO 9915553 A2 WO 1998-DE2896 19980923; DE 19821060 A1 DE 1998-19821060 19980511; AU 9913320 A AU 1999-13320 19980923; EP 1017723 A2 EP 1998-956800 19980923, WO 1998-DE2896 19980923; JP 2001517425 W WO 1998-DE2896 19980923, JP 2000-512857 19980923; AU 752433 B AU 1999-13320 19980923; US 2002177191 A1 Cont of WO 1998-DE2896 19980923, Cont of US 2000-509283 20000811, US 2001-972524 20011004; US 2002182667 A1 Cont of WO 1998-DE2896 19980923, Cont of US 2000-509283 20000811, US 2001-823307 20010402

FDT AU 9913320 A Based on WO 9915553; EP 1017723 A2 Based on WO 9915553; JP 2001517425 W Based on WO 9915553; AU 752433 B Previous Publ. AU 9913320, Based on WO 9915553

PRAI DE 1998-19821060 19980511; DE 1997-19741929 19970923

AB WO 9915553 A UPAB: 19990616

NOVELTY - Polypeptide (I, designated 8F4) co-stimulates T cells, is present on activated CD4+ and CD8+ T cells but not on resting or activated B cells, granulocytes, monocytes, natural killer or dendritic cells, and exists as a dimer of 55-60 kD (by non-reducing sodium dodecylsulfate polyacrylamide gel electrophoresis, SDS-PAGE), with individual chains of 27 and 29 kD (reducing SDS-PAGE).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) polypeptides (Ia) with co-stimulating activity on T cells having at least 40% homology with a 199 amino acid sequence (2; given in the specification) or its biologically active fragments or analogs;

(b) DNA (II) encoding (I) of sequence (2), or its fragments;

(c) plasmids and viral DNA vectors containing (II);

(d) prokaryotic and eukaryotic host cells stably transformed with this plasmid or vector;

(e) recombinant production of (I) or (Ia) by growing these cells;

(f) antibody (Ab) against (I) or (Ia);

(g) hybridomas that produce monoclonal Ab;

(h) use of (I) or (Ia), cells containing them, their inhibitors, or agents that modulate their signal transduction pathways or upregulate them on T cell surfaces as pharmaceuticals; and

(i) use of agents that specifically recognize (I) or (Ia) as diagnostic reagents.

ACTIVITY - For (I), anticancer; antiviral; anti-asthma; for inhibitors of (I), immunomodulatory.

MECHANISM OF ACTION - 8F4 provides a strong co-stimulatory signal for T cell activation, i.e. it amplifies proliferation of T cells, synthesis of certain cytokines and other regulatory agents, and improves T cell-dependent antibody production by B cells. Purified CD8+ T cells were stimulated for 51 hr with a suboptimal concentration of the monoclonal antibody OKT3 in presence of, as co-stimulant, (a) an 8F4-specific antibody or (b) an anti-CD28 antibody, both at 2 mu g/ml. The proliferation of the cells was assessed by incorporation of tritiated

thymidine. Both antibodies were equally effective but the 8F4 antibody did not induce secretion of interleukin-2 (contrast the CD28 antibody).

USE - Agents that inhibit 8F4 are used to treat or prevent autoimmune diseases, to prevent transplant rejection and to treat disorders of immune system regulation. 8F4, or cells that express it, is/are used to treat or prevent cancers, acquired immune deficiency syndrome, asthma and chronic infectious diseases (e.g. hepatitis B or C). Agents that specifically recognize (I), or the nucleic acid encoding it, are used for diagnosis of these disorders.

ADVANTAGE - 8F4 is expressed only on activated T cells, contrast CD28 which is constitutively expressed by T cells.

Dwg.0/16

TECH UPTX: 19990616

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred protein: (Ia) is particularly sequence (2) or its fragments or analogs.

Preferred nucleic acid: (II) is (a) a 2641 bp sequence (1, given in the specification) or its complement, (b) a sequence that hybridizes to (a), or (c) a sequence equivalent to (a) or (b) within the degeneracy of the genetic code.

Preferred antibodies: These are monoclonal and are produced by:
(i) immunizing mice with human T cells that have been activated with both phorbol myristate acetate and the calcium ionophore ionomycin;
(ii) fusing B cells from the mice with a myeloma cell line; and
(iii) selection, then purification, of antibodies from the resulting hybridomas by flow cytometry, selecting for reaction with the activated T cells but not with resting T cells.

Preferred diagnosis: Diagnosis uses (i) RNA or DNA, in usual hybridization and amplification methods, or (b) antibodies, **ligands** or (**ant**)agonists. Standard methods such as enzyme-linked immunosorbent assay, flow cytometry, Western blotting, **radioimmunoassay**, nephelometry or histochemical staining are used.

Preferred Method: Fluorescently **labeled** Ab were used, in flow cytometry, to identify the cell line MOLT-4V as a constitutive producer of 8F4. These cells were grown, lysed and the lysate incubated with affinity material loaded with Ab. Bound 8F4 was eluted, reduced and monomers separated by two-dimensional electrophoresis (reduced and non-reduced). Tryptic fragments from the monomers were sequenced and the information used to design degenerate oligonucleotides for screening a MOLT-4V cDNA library. Six positive clones were sequenced, one contained the 2641 bp sequence. Other independent clones contained sequences that differed in the 3'-untranslated region.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Inhibitors: Inhibitors of 8F4 are monoclonal Ab, natural or synthetic **ligands** or (**ant**)agonists.

L14 ANSWER 8 OF 8 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1997-202171 [18] WPIDS
DNN N1997-167097 DNC C1997-064664
TI Screening compounds for binding to fusion proteins with defined ligands - allows high capacity assays and identification of (ant)agonists or inhibitors for drug development.
DC **B04 D16** K08 **S03**
IN MARCY, A; SALOWE, S P; WISNIEWSKI, D
PA (MERI) MERCK & CO INC
CYC 21
PI WO 9710253 A1 19970320 (199718)* EN 36p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
US 5783398 A 19980721 (199836)

EP 871648 A1 19981021 (199846) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
JP 11513246 W 19991116 (200005) 68p
ADT WO 9710253 A1 WO 1996-US14567 19960911; US 5783398 A Provisional US 1995-3819P 19950915, US 1996-707792 19960904; EP 871648 A1 EP 1996-935808 19960911, WO 1996-US14567 19960911; JP 11513246 W WO 1996-US14567 19960911, JP 1997-512071 19960911
FDT EP 871648 A1 Based on WO 9710253; JP 11513246 W Based on WO 9710253
PRAI GB 1996-5210 19960312; US 1995-3819P 19950915; US 1996-707792 19960904
AB WO 9710253 A UPAB: 19970502
A novel method for screening of compounds which bind to a fusion protein (FP), comprises: (a) mixing a test compound, a tagged ligand, the fusion protein and a **radiolabelled** ligand; (b) adding the mixture to a coated microscintillation plate; (c) incubating the mixture for 1-24 hours; (d) measuring the plate bound counts attributable to the binding of the tagged ligand to the fusion protein in the presence of the test compound using scintillation counting; and (e) determining the binding of the ligand to the fusion protein in the presence of the test compound relative to a control assay run in the absence of the test compound.

USE - The method allows screening for cpds. which bind to a FP contg. a target protein. Functional assays of ligand binding to a single or multiple signal transduction domain(s) are possible, e.g. binding of a phosphopeptide an SH2 domain. Also agonists, antagonists and/or inhibitors for drug development may be identified.

ADVANTAGE - Specialised **radiochemical** synthesis is not required unlike existing methods using short-lived isotopes which require frequent prepn. of material. In contrast to prior art, the method is readily adaptable to robotic automation for high capacity screening.
Dwg.0/1

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=> fil biosis medline
FILE 'BIOSIS' ENTERED AT 10:52:57 ON 18 AUG 2003
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FILE 'MEDLINE' ENTERED AT 10:52:57 ON 18 AUG 2003

=> d his

     (FILE 'WPIDS' ENTERED AT 10:38:32 ON 18 AUG 2003)
               DEL HIS Y

     FILE 'BIOSIS, MEDLINE' ENTERED AT 10:49:52 ON 18 AUG 2003
L1          1538 S  ADENINE NUCLEOTIDE TRANSLOC?
L2         17567 S ANT
L3         18829 S L1 OR L2
L4          1349 S ATRACTYLI# OR ATRACTYLATE OR ATRACTYLOSI?
L5           264 S L4 AND L3
L6           264 S L4 (S) L5
L7            21 S L6 AND LIGAN?
L8            12 DUP REM L7 (9 DUPLICATES REMOVED)

     FILE 'BIOSIS, MEDLINE' ENTERED AT 10:52:57 ON 18 AUG 2003

=> d bib ab it 1-12 l8

L8   ANSWER 1 OF 12  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
     DUPLICATE 1
AN   2002:535619  BIOSIS
DN   PREV200200535619
TI   A novel adenine nucleotide translocase
     inhibitor, MT-21, induces cytochrome c release by a mitochondrial
     permeability transition-independent mechanism.
AU   Machida, Kiyotaka; Hayashi, Yujiro; Osada, Hiroyuki (1)
CS   (1) Antibiotics Laboratory, RIKEN, Hirosawa 2-1, Saitama, 351-0198:
     antibiot@postman.riken.go.jp Japan
SO   Journal of Biological Chemistry, (August 23, 2002) Vol. 277, No. 34, pp.
     31243-31248. http://www.jbc.org/. print.
     ISSN: 0021-9258.
DT   Article
LA   English
AB   The release of cytochrome c from mitochondria is a critical step during
     apoptosis. In order to study this process, we have used a synthetic
     compound, MT-21, that is able to initiate release of cytochrome c from
     isolated mitochondria. We demonstrate that MT-21 significantly inhibits
     ADP transport activity in mitochondria and reduces binding of the
     adenine nucleotide translocase (ANT)
     to a phenylarsine oxide affinity matrix. These results suggest that
     ANT, one of the components of the mitochondrial permeability
     transition (PT) pore, is the molecular target for MT-21. In agreement with
     this, the MT-21-induced cytochrome c release was effectively inhibited in
     the presence of ANT ligands, and MT-21 could
     dissociate ANT from a complex with a glutathione
     S-transferase-cyclophilin D fusion protein. Interestingly, we also found
     that specific inhibitors of ANT such as MT-21 and
     atractyloside could induce cytochrome c release without
     mitochondrial swelling and that this event was highly dependent on the
     presence of Mg2+. These results suggest that although ANT
     resides in the mitochondrial inner membrane, specific ANT
     inhibitors can induce cytochrome c release without having an effect on
```

inner membrane permeability. Therefore, MT-21 can be a powerful tool for studying the mechanism of PT-independent cytochrome c release from mitochondria.

IT Major Concepts
Biochemistry and Molecular Biophysics

IT Parts, Structures, & Systems of Organisms
mitochondria; mitochondrial permeability transition pore

IT Chemicals & Biochemicals
MT-21; S-transferase-cyclophilin D fusion protein; **adenine nucleotide translocase**: inhibition; **atractyloside**; cytochrome c: release; magnesium(II) ion; phenylarsine oxide

RN 17754-44-8 (**ATRACTYLOSIDE**)
9007-43-6 (CYTOCHROME C)
22537-22-0 (MAGNESIUM(II) ION)
637-03-6 (PHENYLARSINE OXIDE)

L8 ANSWER 2 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2

AN 2002:185174 BIOSIS

DN PREV200200185174

TI Cytochrome c oxidase subunit III. A molecular marker for N-(4-hydroxyphenyl)retinamide-induced oxidative stress in hepatoma cells.

AU You, Kyung-Ran; Wen, Jing; Lee, Soo-Taek; Kim, Dae-Ghon (1)

CS (1) Division of Gastroenterology and Hepatology, Dept. of Internal Medicine, Chonbuk National University Medical School and Hospital, 634-18 Keumam-dong, Dukjin-ku, Chonju, Chonbuk, 561-712: daeghon@moak.chonbuk.ac.kr South Korea

SO Journal of Biological Chemistry, (February 8, 2002) Vol. 277, No. 6, pp. 3870-3877. http://www.jbc.org/. print.
ISSN: 0021-9258.

DT Article

LA English

AB N-(4-hydroxyphenyl)retinamide (4HPR), a chemopreventive and chemotherapeutic retinoid, induces apoptosis in various types of cells. Currently, oxidative mitochondrial damage is thought to cause 4HPR-induced apoptosis, although the exact mechanism has not yet been clarified. 4HPR effectively induces apoptosis in hepatoma cells although the susceptibility differs in a cell-specific manner. Hep-3B and PLC/PRF/5 cells were more susceptible to 4HPR than were Hep-G2 and SK-HEP-1 cells, and the resistance to 4HPR seems to be related to growth inhibition (G1 arrest). We further observed that 4HPR specifically down-regulates cytochrome c oxidase subunit III (CO III) transcript levels through destabilization of its mRNA and thus decreases the activity of cytochrome c oxidase (complex IV). To explore the mechanism whereby the CO III transcript was decreased by 4HPR, we used **adenine nucleotide translocator (ANT) ligands**, which modulate mitochondrial transmembrane potential (DELTApsim) without altering CO III transcription. Intriguingly, bongkrekic acid, a specific **ANT** inhibitor, enhanced 4HPR-induced DELTApsim disruption, which in turn decreased the level of CO III transcripts, which was accompanied by increases in the generation of reactive oxygen species and in apoptosis. In contrast, **atractyloside**, an activator of **ANT**, inhibited those 4HPR-induced effects. Taken together, these results indicate that down-regulation of CO III, a molecular marker of oxidative stress, may result from upstream DELTApsim disruption and that **ligands** of **ANT** may be capable of modulating 4HPR-induced oxidative stress and apoptosis.

IT Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular Biophysics);

Molecular Genetics (Biochemistry and Molecular Biophysics)
IT Chemicals & Biochemicals
N-(4-hydroxyphenyl)retinamide; **adenine nucleotide translocator ligands** [**ANT ligands**]; **atractyloside**; bongkrekic acid; cytochrome c oxidase: mRNA destabilization, subunit III; mRNA [messenger RNA]
IT Miscellaneous Descriptors
apoptosis; oxidative stress
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hep-3B cell line (Hominidae): human hepatoma cells; Hep-G2 cell line (Hominidae): human hepatoma cells; PLC/PRF/5 cell line (Hominidae): human hepatoma cells; SK-HEP-1 cell line (Hominidae): human hepatoma cells
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 65646-68-6 (N-(4-HYDROXYPHENYL)RETINAMIDE)
17754-44-8 (**ATRACTYLOSIDE**)
11076-19-0 (BONGKREKIC ACID)
9001-16-5 (CYTOCHROME C OXIDASE)

L8 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 2002:120145 BIOSIS
DN PREV200200120145
TI **Ligand**-selective modulation of the permeability transition pore by arginine modification. Opposing effects of p-hydroxyphenylglyoxal and phenylglyoxal.
AU Linder, Matts D.; Morkunaite-Haimi, Sarune; Kinnunen, Paavo K. J.; Bernardi, Paolo; Eriksson, Ove (1)
CS (1) Institute of Biomedicine/Biochemistry, University of Helsinki, Haartmaninkatu 8, Helsinki, FIN-00014: ove.eriksson@helsinki.fi Finland
SO Journal of Biological Chemistry, (January 11, 2002) Vol. 277, No. 2, pp. 937-942. http://www.jbc.org/. print.
ISSN: 0021-9258.
DT Article
LA English
AB Chemical modification of mitochondria with the arginine-specific reagents phenylglyoxal (PGO) and 2,3-butanedione (BAD) decreases the Ca2+ sensitivity of the permeability transition pore (PTP) and stabilizes it in the closed conformation (Eriksson, O., Fontaine, E., and Bernardi, P. (1998) J. Biol. Chem. 273, 12669-12674). Unexpectedly, modification of mitochondria with the arginine-specific reagent p-hydroxyphenylglyoxal (OH-PGO) resulted instead in PTP opening. Sequential modification with OH-PGO and PGO (or BAD) revealed that the effects on the PTP depended on the order of the additions. PTP opening was observed when OH-PGO preceded, and PTP closing was observed when OH-PGO followed, the addition of PGO (or BAD). The differential effects of OH-PGO and PGO on the PTP open probability (i) were not modified by the conformation-specific **ligands** of the **adenine nucleotide translocase** bongkrekate and **atractylate**; and (ii) were also observed in de-energized mitochondria, indicating that the effect is exerted directly on the PTP. OH-PGO dramatically sensitized PTP opening, which was triggered by depolarization even in the presence of EGTA. These data show that arginine modification modulates the PTP conformation in a **ligand**-selective fashion and suggest that the effects of OH-PGO, PGO, and BAD are mediated by the same arginine residues. We analyzed the structure of the arginine adducts by matrix-assisted laser desorption ionization and time-of-flight mass spectrometry using a test peptide and

N-acetylarginine. The results indicate that both OH-PGO and PGO react with arginine at a stoichiometry of 2:1 and form stable adducts that may be feasible to identify the PTP at the molecular level.

IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques

IT Parts, Structures, & Systems of Organisms
liver: digestive system; mitochondria

IT Chemicals & Biochemicals
2,3-butanedione [BAD]; N-acetylarginine; **adenine nucleotide translocase** bongkrekate; arginine; arginine adducts: analysis, structure; **atractylate**; p-hydroxyphenylglyoxal; permeability transition pore [PTP]: calcium(II) ion sensitivity, closed conformation, **ligand**-selective modulation; phenylglyoxal [PGO]; test peptide

IT Methods & Equipment
Bruker Biflex III spectrometer: Bruker, laboratory equipment; arginine modification: Synthetic Techniques, synthetic method; chemical modification: Synthetic Techniques, synthetic method; matrix-assisted laser desorption ionization time-of-flight mass spectrometry [MALDI-TOF MS]: Spectrum Analysis Techniques, analytical method; sequential modification: Synthetic Techniques, synthetic method

IT Miscellaneous Descriptors
depolarization

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Wistar rat (Muridae): male

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

RN 431-03-8 (2,3-BUTANEDIONE)
74-79-3Q (ARGININE)
7200-25-1Q (ARGININE)
24645-80-5 (P-HYDROXYPHENYLGLYOXAL)
1074-12-0 (PHENYLGLYOXAL)

L8 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4

AN 2000:114118 BIOSIS

DN PREV200000114118

TI Bcl-2 and Bax regulate the channel activity of the mitochondrial **adenine nucleotide translocator.**

AU Brenner, Catherine; Cadiou, Herve; Vieira, Helena L. A.; Zamzami, Naoufal; Marzo, Isabel; Xie, Zhihua; Leber, Brian; Andrews, David; Duclohier, Herve; Reed, John C.; Kroemer, Guido (1)

CS (1) 19 Rue Guy Moquet, F-94801, Villejuif France

SO Oncogene, (Jan. 20, 2000) Vol. 19, No. 3, pp. 329-336.
ISSN: 0950-9232.

DT Article

LA English

SL English

AB Bcl-2 family protein including anti-apoptotic (Bcl-2) or pro-apoptotic (Bax) members can form ion channels when incorporated into synthetic lipid bilayers. This contrasts with the observation that Bcl-2 stabilizes the mitochondrial membrane barrier function and inhibits the permeability transition pore complex (PTPC). Here we provide experimental data which may explain this apparent paradox. Bax and **adenine nucleotide translocator** (**ANT**), the most abundant inner mitochondrial membrane protein, can interact in artificial lipid bilayers to yield an efficient composite channel whose

electrophysiological properties differ quantitatively and qualitatively from the channels formed by Bax or **ANT** alone. The formation of this composite channel can be observed in conditions in which Bax protein alone has no detectable channel activity. Cooperative channel formation by Bax and **ANT** is stimulated by the **ANT ligand atractyloside** (Atr) but inhibited by ATP, indicating that it depends on the conformation of **ANT**. In contrast to the combination of Bax and **ANT**, **ANT** does not form active channels when incorporated into membranes with Bcl-2. Rather, **ANT** and Bcl-2 exhibit mutual inhibition of channel formation. Bcl-2 prevents channel formation by Atr-treated **ANT** and neutralizes the cooperation between Bax and **ANT**. Our data are compatible with a menage a trois model of mitochondrial apoptosis regulation in which **ANT**, the likely pore forming protein within the PTPC, interacts with Bax or Bcl-2 which influence its pore forming potential in opposing manners.

IT Major Concepts
Cell Biology

IT Chemicals & Biochemicals
mitochondrial **adenine nucleotide translocator**: Bax protein regulation, Bcl-2 protein regulation, channel activity

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Rat-1 cell line (Muridae): rat fibroblast cell line

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

L8 ANSWER 5 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5

AN 2000:382167 BIOSIS

DN PREV200000382167

TI The anti-oxidant ebselen antagonizes the release of the apoptogenic factor cytochrome c induced by Fe2+/citrate in rat liver mitochondria.

AU Boireau, Alain (1); Marechal, Pierre-Alain; Meunier, Mireille; Dubedat, Pierre; Moussaoui, Saliha

CS (1) Departement Biologie, Centre de Recherche de Vitry-Alfortville, Aventis Pharma S.A., 13 quai Jules Guesde, 94403, Vitry-sur-Seine Cedex France

SO Neuroscience Letters, (August 4, 2000) Vol. 289, No. 2, pp. 95-98. print. ISSN: 0304-3940.

DT Article

LA English

SL English

AB We studied the effects of ebselen (a seleno-organic anti-oxidant), on the release of the apoptogenic factor, cytochrome c, in two different experimental situations damaging mitochondria: (1) Fe2+/citrate, known to induce lipid peroxidation consecutively to an oxidative stress; and (2) **atractyloside**, a **ligand** of the **adenine nucleotide translocator**. The effects of ebselen were compared to those of butylated hydroxytoluene (BHT, an inhibitor of lipid peroxidation), and cyclosporine A (CsA, a classical pore antagonist). Ebselen, like BHT, inhibited Fe2+/citrate-induced release of cytochrome c, whereas CsA was inactive. On the contrary, neither ebselen nor BHT inhibited **atractyloside**-induced release of cytochrome c, whereas CsA was potently active. The antioxidant properties of ebselen may protect mitochondria from the consequences of the release of cytochrome c. Thus, it is suggested that the neuroprotective effect of ebselen previously

demonstrated in humans and in animals may be due, at least in part, to a mitochondrial protection.

IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)

IT Parts, Structures, & Systems of Organisms
liver mitochondria: digestive system

IT Chemicals & Biochemicals
cytochrome c: apoptogenic factor, release; ebselen: antioxidant, neuroprotective effect; iron/citrate: induced

ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
rat (Muridae)

ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates

RN 9007-43-6 (CYTOCHROME C)
60940-34-3 (EBSELEN)
2338-05-8 (IRON/CITRATE)

L8 ANSWER 6 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6

AN 1998:475916 BIOSIS

DN PREV199800475916

TI Bax and **adenine nucleotide translocator** cooperate in the mitochondrial control of apoptosis.

AU Marzo, Isabel; Brenner, Catherine; Zamzami, Naoufal; Juergensmeier, Juliane M.; Susin, Santos A.; Vieira, Helena L. A.; Prevost, Marie-Christine; Xie, Zhihua; Matsuyama, Shigemi; Reed, John C.; Kroemer, Guido (1)

CS (1) CNRS, UPR 420, 19 rue Guy Moquet, F-94801 Villejuif France

SO Science (Washington D C), (Sept. 25, 1998) Vol. 281, No. 5385, pp. 2027-2031.
ISSN: 0036-8075.

DT Article

LA English

AB The proapoptotic Bax protein induces cell death by acting on mitochondria. Bax binds to the permeability transition pore complex (PTPC), a composite proteaceous channel that is involved in the regulation of mitochondrial membrane permeability. Immunodepletion of Bax from PTPC or purification of PTPC from Bax-deficient mice yielded a PTPC that could not permeabilize membranes in response to **atractyloside**, a proapoptotic **ligand** of the **adenine nucleotide translocator** (**ANT**). Bax and **ANT** coimmunoprecipitated and interacted in the yeast two-hybrid system. Ectopic expression of Bax induced cell death in wild-type but not in **ANT**-deficient yeast. Recombinant Bax and purified **ANT**, but neither of them alone, efficiently formed **atractyloside**-responsive channels in artificial membranes. Hence, the proapoptotic molecule Bax and the constitutive mitochondrial protein **ANT** cooperate within the PTPC to increase mitochondrial membrane permeability and to trigger cell death.

IT Major Concepts
Cell Biology

IT Parts, Structures, & Systems of Organisms
mitochondria; mitochondrial membrane

IT Chemicals & Biochemicals
adenine nucleotide translocator; Bax: proapoptotic stimulator, protein

IT Miscellaneous Descriptors
apoptosis control
ORGN Super Taxa
Fungi: Plantae
ORGN Organism Name
yeast (Fungi)
ORGN Organism Superterms
Fungi; Microorganisms; Nonvascular Plants; Plants

L8 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 7
AN 1998:343950 BIOSIS
DN PREV199800343950
TI PK11195, a **ligand** of the mitochondrial benzodiazepine receptor, facilitates the induction of apoptosis and reverses Bcl-2 mediated cytoprotection.
AU Hirsch, Tamara; Decaudin, Didier; Susin, Santos A.; Marchetti, Philippe; Larochette, Nathanael; Resche-Rigon, Michele; Kroemer, Guido (1)
CS (1) 19 rue Guy Moquet, B.P. 8, F-94801 Villejuif France
SO Experimental Cell Research, (June 15, 1998) Vol. 241, No. 2, pp. 426-434. ISSN: 0014-4827.
DT Article
LA English
AB One critical step of the apoptotic process is the opening of the mitochondrial permeability transition (PT) pore leading to the disruption of mitochondrial membrane integrity. and to the dissipation of the inner transmembrane proton gradient (DELTAPSIm). The mitochondrial PT pore is a polyprotein structure which is inhibited by the apoptosis-inhibitory oncoprotein Bcl-2 and which is closely associated with the mitochondrial benzodiazepine receptor (mBzR). Here we show that PH11195, a prototypic **ligand** of the 18-kDa mBzR, facilitates the induction of DELTAPSIm disruption and subsequent apoptosis by a number of different agents, including agonists of the glucocorticoid receptor, chemotherapeutic agents (etoposide, doxorubicin), gamma irradiation, and the proapoptotic second messenger ceramide. Whereas PK11195 itself has no cytotoxic effect, it enhances apoptosis induction by these agents. This effect is not observed for benzodiazepine diazepam, whose binding site in the mBzR differs from PK11195. PK11195 partially reverses Bcl-2 mediated inhibition of apoptosis in two different cell lines. Thus, transfection-enforced Bcl-2 overexpression confers protection against glucocorticoids and chemotherapeutic agents, and this protection is largely reversed by the addition of PK11195. This effect is observed at the level of DELTAPSIm dissipation as well as at the level of nuclear apoptosis. To gain insights into the site of action of PK11195, we performed experiments on isolated organelles. PK11195 reverses the Bcl-2-mediated mitochondrial retention of apoptogenic factors which cause isolated nuclei to undergo apoptosis in a cell-free system. Mitochondria from control cells, but not mitochondria from Bcl-2-overexpressing cells, readily release such apoptogenic factors in response to **atractyloside**, a **ligand** of the **adenine nucleotide translocator**. However, control and Bcl-2-overexpressing mitochondria respond equally well to a combination of **atractyloside** and PK11195. Altogether, these findings indicate that PK11195 abolishes apoptosis inhibition by Bcl-2 via a direct effect on mitochondria. Moreover, they suggest a novel strategy for enhancing the susceptibility of cells to apoptosis induction and, concomitantly, for reversing Bcl-2-mediated cytoprotection.
IT Major Concepts
Cell Biology
IT Chemicals & Biochemicals
mitochondrial benzodiazepine receptor; Bcl-2; PK11195

IT Miscellaneous Descriptors
apoptosis; cytoprotection; mitochondrial membrane integrity
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mice (Muridae)
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 85532-75-8 (PK11195)
12794-10-4 (BENZODIAZEPINE)

L8 ANSWER 8 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8
AN 1996:270446 BIOSIS
DN PREV199698826575
TI Apoptosis-associated derangement of mitochondrial function in cells lacking mitochondrial DNA.
AU Marchetti, Philippe; Susin, Santos A.; Decaudin, Didier; Gamen, Susana; Castedo, Maria; Hirsch, Tamra; Zamzami, Naoufal; Naval, Javier; Senik, Anna; Kroemer, Guido (1)
CS (1) CNRS-UPR420, 19 rue Guy Moquet, B.P. 8, F-94801 Villejuif France
SO Cancer Research, (1996) Vol. 56, No. 9, pp. 2033-2038.
ISSN: 0008-5472.
DT Article
LA English
AB U937 cells lacking mitochondrial DNA (rho degree cells) are auxotrophic for uridine and pyruvate, hypersensitive to hypoglycemic conditions, and resistant to antimycin A-induced apoptosis. In spite of their obvious metabolic defects, rho degree cells possess a normal mitochondrial transmembrane potential, as well as a near-normal capacity to generate superoxide anion after menadione treatment. Similarly to rho+ controls, rho degree cells undergo apoptosis in response to tumor necrosis factors plus cycloheximide. Detailed comparison of the apoptotic process in rho degree and rho degree cells reveals essentially the same sequence of events. In response to tumor necrosis factor/cycloheximide, cells first lose their mitochondrial transmembrane potential (DELTA--psi-m) and then manifest late apoptotic alterations, such as generation of reactive oxygen species and DNA fragmentation. Experiments involving isolated mitochondria from rho+ and rho degree cells confirm that rho degree mitochondria can be induced to undergo permeability transition, a process thought to account for the pre-apoptotic DELTA--psi-m disruption in cells. Like rho+ mitochondria, rho degree mitochondria contain a pre-formed soluble factor that is capable of inducing chromatin condensation in isolated nuclei in vitro. This factor is released from mitochondria upon induction of permeability transition by calcium or the specific **ligand** of the **adenine nucleotide translocator** **atractyloside**. In conclusion, it appears that all structures involved in the maintenance and pre-apoptotic disruption of the DELTA--psi-m, as well as a mitochondrial apoptotic factor(s), are present in rho degree cells and thus are controlled by the nuclear rather than by the mitochondrial genome. These findings underline the contribution of mitochondria to the apoptotic process.
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Hematology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Pathology
IT Chemicals & Biochemicals
URIDINE; PYRUVATE; SUPEROXIDE

IT Miscellaneous Descriptors
CHROMATIN; DNA FRAGMENTATION; HUMAN U937 LYMPHOMA CELLS; PYRUVATE; SUPEROXIDE ANION; TUMOR NECROSIS FACTOR-ALPHA; URIDINE
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
RN 58-96-8 (URIDINE)
57-60-3 (PYRUVATE)
11062-77-4 (SUPEROXIDE)

L8 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 9
AN 1996:282888 BIOSIS
DN PREV199699005244
TI Mitochondrial control of nuclear apoptosis.
AU Zamzami, Naoufal; Susin, Santos A.; Marchetti, Philippe; Hirsch, Tamara; Gomez-Monterrey, Isabel; Castedo, Maria; Kroemer, Guido (1)
CS (1) CNRS-UPR420, 19 rue Guy Moquet, B.P.8, F-94801 Villejuif France
SO Journal of Experimental Medicine, (1996) Vol. 183, No. 4, pp. 1533-1544. ISSN: 0022-1007.
DT Article
LA English
AB Anucleate cells can be induced to undergo programmed cell death (PCD), indicating the existence of a cytoplasmic PCD pathway that functions independently from the nucleus. Cytoplasmic structures including mitochondria have been shown to participate in the control of apoptotic nuclear disintegration. Before cells exhibit common signs of nuclear apoptosis (chromatin condensation and endonuclease-mediated DNA fragmentation), they undergo a reduction of the mitochondrial transmembrane potential (DELTA--PSI-m) that may be due to the opening of mitochondrial permeability transition (PT) pores. Here, we present direct evidence indicating that mitochondrial PT constitutes a critical early event of the apoptotic process. In a cell-free system combining purified mitochondria and nuclei, mitochondria undergoing PT suffice to induce chromatin condensation and DNA fragmentation. Induction of PT by pharmacological agents augments the apoptosis-inducing potential of mitochondria. In contrast, prevention of PT by pharmacological agents impedes nuclear apoptosis, both in vitro and in vivo. Mitochondria from hepatocytes or lymphoid cells undergoing apoptosis, but not those from normal cells, induce the disintegration of isolated Hela nuclei. A specific **ligand** of the mitochondrial **adenine nucleotide translocator** (**ANT**), bongkrekic acid, inhibits PT and reduces apoptosis induction by mitochondria in a cell-free system. Moreover, it inhibits the induction of apoptosis in intact cells. Several pieces of evidence suggest that the proto-oncogene product Bcl-2 inhibits apoptosis by preventing mitochondrial PT. First, to inhibit nuclear apoptosis, Bcl-2 must be localized in mitochondrial but not in nuclear membranes. Second, transfection-enforced hyperexpression of Bcl-2 directly abolishes the induction of mitochondrial PT in response to a protonophore, a pro-oxidant, as well as to the **ANT ligand atractyloside**, correlating with its apoptosis-inhibitory effect. In conclusion, mitochondrial PT appears to be a critical step of the apoptotic cascade.
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Development; Genetics; Membranes (Cell Biology);

Metabolism; Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics); Pathology; Physiology
IT Miscellaneous Descriptors
APOPTOTIC CASCADE; CHROMATIN CONDENSATION; DNA FRAGMENTATION; HUMAN CELL LINES; MITOCHONDRIAL PERMEABILITY TRANSITION PORES; PROGRAMMED CELL DEATH
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae); Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates

L8 ANSWER 10 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1983:258433 BIOSIS
DN BA76:15925
TI STUDIES ON THE INTERACTION OF PALMITOYL COENZYME A WITH THE **ADENINE NUCLEOTIDE TRANSLOCASE.**
AU WOLDEGIORGIS G; YOUSUFZAI S Y K; SHRAGO E
CS DEPARTMENT OF MEDICINE, UNIVERSITY OF WISCONSIN, MADISON, WISCONSIN 53706.
SO J BIOL CHEM, (1982 (RECD 1983)) 257 (24), 14783-14787.
CODEN: JBCHA3. ISSN: 0021-9258.
FS BA; OLD
LA English
AB Palmitoyl-CoA, which can inhibit adenine nucleotide transport from both the cytosolic and matrix sides of the inner mitochondrial membrane, was observed to remove bound [14C]ADP from the cytosolic side of intact beef heart mitochondria but not from the matrix side of submitochondrial particles with inverted sidedness. The ADP-stimulated binding of [14C]N-ethylmaleimide to mitochondria, which can be prevented by **atractylate**, was also inhibited by palmitoyl-CoA with isolated mitochondria but not submitochondrial particles. Two analogs of palmitoyl-CoA were synthesized and tested for their ability to inhibit **adenine nucleotide translocation** in mitochondria and submitochondrial particles. 1,N6-ethenopalmitoyl-CoA closely resembled palmitoyl-CoA in its action, whereas dephosphopalmitoyl-CoA was completely ineffective at the same concentration. Mitochondria and submitochondrial particles were incubated with [14C]palmitoyl-CoA and the [14C]palmitoyl-CoA-protein complexes were purified by extraction with Triton X-100 and hydroxyapatite chromatography. The elution profiles of radioactivity and protein resembled those obtained with radioactive carboxyatractylate and bongkrekic acid and represent the purified ADP/ATP carrier. The palmitoyl-CoA **ligand** conferred stability on the protein, particularly against trypsin digestion, when the palmitoyl-CoA protein complex was purified from isolated mitochondria. However, when the protein complex was purified from submitochondrial particles, palmitoyl-CoA was less able to prevent trypsin digestion. Again, these characteristics are similar to those of the respective carboxyatractylate and bongkrekic acid protein complexes. These results indicate a site-specific interaction of palmitoyl-CoA with the ADP/ATP carrier and support the concept that long chain fatty acyl-CoA esters are natural **ligands** for the carrier.
IT Miscellaneous Descriptors
BEEF HEART MITOCHONDRIA SUB MITOCHONDRIAL PARTICLES ADP ATP CARRIER CARBOXY **ATRACTYLATE** BONGKREKIC-ACID
RN 1763-10-6 (PALMITOYL COENZYME A)
9068-80-8 (**ADENINE NUCLEOTIDE TRANSLOCASE**)
11076-19-0 (BONGKREKIC-ACID)

L8 ANSWER 11 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1979:204356 BIOSIS
DN BA68:6860
TI PHOSPHATE DEPENDENCE AND **ATRACTYLOSIDE** INHIBITION OF MITOCHONDRIAL OXIDATIVE PHOSPHORYLATION THE ADP ATP CARRIER IS RATE LIMITING.
AU LEMASTERS J J; SOWERS A E
CS LAB. CELL BIOL., DEP. ANAT., UNIV. N.C., CHAPEL HILL, N.C. 27514, USA.
SO J BIOL CHEM, (1979) 254 (4), 1248-1251.
CODEN: JBCHA3. ISSN: 0021-9258.
FS BA; OLD
LA English
AB ATP production and O2 consumption by rat liver mitochondria were measured as a function of **atractyloside** and Pi concentration. The "on" kinetics of **atractyloside** inhibition of ATP production are very rapid. The onset of inhibitory effect is complete within 1 s, even at concentrations which produce partial inhibition. A **ligand** conservation plot relating **atractyloside** concentration and fractional inhibition of ATP production is linear and indicates that inhibition is proportional to the fraction of ADP-ATP carier sites bound with **atractyloside**. Estimates of E, the number of **atractyloside** sensitive sites and Ki, the **atractyloside** inhibition constant, are 3.8 .times. 10-7 mol/g of protein and 2.2 .times. 10-8 M, respectively. Mitochondrial respiration during active oxidative phosphorylation is proportional to log [Pi]. Plots of **atractyloside** concentration vs. respiratory rate at different Pi concentrations are similar in shape. There is no increase in sigmoidicity with decreasing Pi that would suggest that the ADP-ATP carrier is losing any rate-limiting character as Pi decreases and the rate of the reaction falls. Hexokinase at concentrations below about 400 units/g of mitochondrial protein limits the rate of mitochondrial respiration with glucose and ATP. **Atractyloside** inhibition curves become increasingly sigmoidal as hexokinase is decreased below 400 units/g of protein. When the ADP-ATP carrier is not rate-limiting, significant amounts of **atractyloside** can bind without producing a corresponding decrease in ATP production. In rat liver mitochondria, **adenine nucleotide translocation** is apparently rate-limiting in the overall reaction of oxidative phosphorylation. It is responsible for the phenomenon of respiratory control.
IT Miscellaneous Descriptors
RAT LIVER METABOLIC-DRUG
RN 14265-44-2 (PHOSPHATE)
17754-44-8 (**ATRACTYLOSIDE**)

L8 ANSWER 12 OF 12 MEDLINE on STN
AN 78103240 MEDLINE
DN 78103240 PubMed ID: 623652
TI The **adenine nucleotide translocator** in foetal, suckling and adult rat liver mitochondria.
AU Pollack J K; Sutton R
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1978 Jan 13) 80 (1) 193-8.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197803
ED Entered STN: 19900314

Last Updated on STN: 19900314
Entered Medline: 19780329